Prevalence of systolic inter-arm differences in blood pressure for different primary care populations: systematic review and meta-analysis

Christopher E Clark, Rod S Taylor, Angela C Shore and John L Campbell

INTRODUCTION

A difference in blood pressure measurements between arms has been reported in cohorts with hypertension, diabetes, chronic kidney disease, or peripheral arterial disease. Inter-arm differences in blood pressure can cause errors in blood pressure interpretation and management when not recognised. They are also associated with increased cardiovascular mortality and morbidity.

The reported prevalences of inter-arm differences vary greatly; they are usually higher in the presence of hypertension. The majority of reports are based on selected or convenience samples, usually in a secondary care setting; fewer studies have addressed the subject in populations relevant to primary care. Various prevalence figures have been reported in cohorts with hypertension, diabetes, chronic kidney disease, or peripheral arterial disease. Differences in blood pressure can cause errors in blood pressure interpretation and management when not recognised. They are also associated with increased cardiovascular mortality and morbidity.

METHOD

MEDLINE, Embase, and Cinahl databases were searched from their respective commencement dates to 12 November 2014 using search terms refined from previous systematic reviews. Further studies were identified from personal archives and checking of reference lists for included studies. Full texts were retrieved for any studies reporting on inter-arm differences in blood pressure. Studies were selected or convenience samples, usually in a secondary care setting; fewer studies have addressed the subject in populations relevant to primary care. Various prevalence figures have been reported in cohorts with hypertension, diabetes, chronic kidney disease, or peripheral arterial disease. Differences in blood pressure can cause errors in blood pressure interpretation and management when not recognised. They are also associated with increased cardiovascular mortality and morbidity.

RESULTS

Eighth IAD studies were identified. Sixteen met inclusion criteria: pooled estimates of prevalence for systolic IAD ≥10 mmHg were 11.2% (95% confidence interval [CI] = 9.1 to 13.6) in hypertension, 7.4% (95% CI = 5.8 to 9.2) in diabetes, and 3.6% (95% CI = 2.3 to 5.0) for a general adult population (P = 0.001 for subgroup differences). Differences persisted for higher cut-off values. Prevalences were lower for East Asian than for Western populations and were overestimated by sequential measurement where this could be compared with simultaneous measurement within studies (relative risk for IAD: 2.9 [95% CI = 2.1 to 4.1]). Studies with higher mean absolute systolic pressures had higher prevalences for a systolic IAD ≥10 mmHg (P = 0.04).

CONCLUSION

Prevalences of IADs rise in relation to underlying cardiovascular comorbidities of the population studied, and are overestimated threefold when sequential measurement is used. Population-specific variation in prevalences of IAD should be taken into account in delivering clinical care and in planning future studies.

Keywords

blood pressure determination; hypertension; prevalence; inter-arm difference; primary care.
method of blood pressure measurement and sampling of the population ensured that study quality for the outcome of interest was standardised.

Study populations were classified as hypertensive, diabetic, or general. Cohorts were included within the general population category unless specifically selected by diabetic or hypertensive status, thus being considered representative of a general primary care population. Where mixed cohorts were reported, authors were contacted to clarify appropriate classification and request subgroup prevalence data.

Study-level prevalence data were extracted from included studies for systolic inter-arm differences ≥10 mmHg, ≥15 mmHg, and ≥20 mmHg. Pooled estimates of mean prevalences for systolic inter-arm differences ≥10 mmHg, ≥15 mmHg, and ≥20 mmHg were calculated and compared between populations using meta-analysis of proportions undertaken in Stata (version 12.1) with the ‘metaprop’ command. A random effects model was chosen due to potential clinical heterogeneity of included studies. Statistical heterogeneity was assessed using the I² statistic and, where present, explored with sensitivity analyses based on ethnic origin, or methodology. Univariable and multivariable meta-regression analyses were undertaken to examine the association between various study-level factors (mean age, percentage of males, mean absolute systolic blood pressure, setting [community versus clinic], country of conduct, and indication [hypertensive versus diabetic versus general population]), and the prevalence for systolic inter-arm differences ≥10 mmHg. The ‘permute’ option for the ‘metareg’ command in Stata was used to allow for multiple testing.

Where studies also reported prevalence of blood pressure differences based on sequential measurements, these data were also extracted for comparison. Differences in aggregate study prevalence were estimated for the simultaneous versus sequential methods after adjustment for within-person correlations reported elsewhere, according to Cochrane Review methods. Results are expressed as relative risks of diagnosing an inter-arm difference for sequential versus simultaneous assessment and pooled using random effects meta-analysis. Potential publication bias was assessed using funnel plots and the Egger test.

RESULTS

Searches identified 12 217 unique citations; 80 full texts were reviewed, and 18 studies met the inclusion criteria. One study reported no prevalence data in a form that could be included in the analysis, and another that rounded inter-arm differences to the nearest 5 mmHg was excluded. Thus 16 studies (comprising 21 subgroups) contributed data to the meta-analyses (Figure 1, Table 1).

Pooled prevalences of a systolic inter-
## Table 1. Studies included in analyses

<table>
<thead>
<tr>
<th>Study (country of origin)</th>
<th>Study population</th>
<th>Method of measurement</th>
<th>Sample size</th>
<th>Prevalence of systolic differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harrison et al 1960[^1] [US]</td>
<td>Patients attending clinic</td>
<td>Simultaneous three pairs of measurements</td>
<td>447</td>
<td>5.3% ≥ 10 mmHg \ 0.1% ≥ 20 mmHg</td>
</tr>
<tr>
<td>Orme et al 1999[^2] [UK]</td>
<td>Staff, visitors, and non-cardiovascular day case surgery patients at one district general hospital. Subjects without cardiovascular disease, mean age 49.1 years (20–89), 43% female</td>
<td>Two automated machines in simultaneous 2 × 2 crossover design; mean of four pairs of readings</td>
<td>364</td>
<td>5.2% ≥ 10 mmHg \ 0 ≥ 20 mmHg</td>
</tr>
<tr>
<td>Kimura et al 2004[^3] [Japan]</td>
<td>Participants in community check-up for arteriosclerosis, age 62.4 years (11.1; 338 male, 702 female)</td>
<td>Simultaneous four-limb machine: ABI-form device (COLIN VP1000); single reading</td>
<td>1090</td>
<td>9.1% &gt; 10 mmHg</td>
</tr>
<tr>
<td>Karagiannis et al 2005[^4] [Greece]</td>
<td>Hospital staff, visitors, and patients, mean age 54 years (18.3); 195 (50.8%) female</td>
<td>Two Omron HEM 705CP in simultaneous 2 × 2 crossover design; mean of four pairs of readings</td>
<td>384</td>
<td>3.4% &gt; 10 mmHg</td>
</tr>
<tr>
<td>Clark et al 2005[^5] [UK]</td>
<td>Primary care hypertensive patients, age 69.6 years (9.7); 40 male</td>
<td>Two Omron HEM 705CP in simultaneous 2 × 2 crossover design; mean of four pairs of readings</td>
<td>94</td>
<td>19% ≥ 10 mmHg \ 6.4% ≥ 15 mmHg</td>
</tr>
<tr>
<td>Kleefstra et al 2007[^6] [Netherlands]</td>
<td>Patients with type 2 diabetes mellitus</td>
<td>Mean of two simultaneous pairs of readings with 2 × Omron M5-1 automated machines</td>
<td>169</td>
<td>9% ≥ 10 mmHg</td>
</tr>
<tr>
<td>Clark et al 2009[^7] [UK]</td>
<td>Subjects with type 2 diabetes mellitus recruited from five general practice surgeries</td>
<td>Two Omron HEM 705CP in simultaneous 2 × 2 crossover design; mean of four pairs of readings</td>
<td>101</td>
<td>10% ≥ 10 mmHg \ 4% ≥ 15 mmHg</td>
</tr>
<tr>
<td>Lohmann et al 2011[^8] [Germany]</td>
<td>Hospital outpatients with one or two cardiovascular risk factors; 76% hypertensive</td>
<td>Simultaneous Microlife WatchBP® Office; mean of three pairs of measurements</td>
<td>118</td>
<td>10% ≥ 10 mmHg</td>
</tr>
<tr>
<td>Fonseca-Reyes et al 2012[^9] [Mexico]</td>
<td>Patients attending hospital hypertension clinics</td>
<td>Two Omron HEM 725 CIC automatic sphygmomanometers, swapped after first pair of readings; mean of two pairs</td>
<td>111</td>
<td>20.7% &gt;5 mmHg \ 13.5% &gt;10 mmHg \ 1.8% &gt;20 mmHg</td>
</tr>
<tr>
<td>Kim 2013[^10] [Korea]</td>
<td>Adult family medicine clinic patients age &gt;40 years free of cardiovascular and renal disease, 200 (43%) with hypertension</td>
<td>Two pairs of simultaneous measurements with 2 × Omron MX3</td>
<td>261 males \ 203 females</td>
<td>1.9% ≥ 10 mmHg \ 0% ≥ 10 mmHg</td>
</tr>
<tr>
<td>Okada et al 2013[^11] [Japan]</td>
<td>Consecutive patients with type 2 diabetes in outpatient clinic</td>
<td>Simultaneous four-limb measurement (COLIN waveform analyser; device not stated.)</td>
<td>314</td>
<td>5.1% ≥ 10 mmHg</td>
</tr>
<tr>
<td>Sheng et al 2013[^12] [China]</td>
<td>Older Chinese (age &gt;60 years), 1895 (60.5%) with hypertension and 285 (9.2%) with diabetes</td>
<td>Simultaneous four-limb machine; ABI-form device (COLIN VP1000)</td>
<td>3133</td>
<td>6.4% ≥ 10 mmHg \ 1.8% ≥ 15 mmHg</td>
</tr>
<tr>
<td>Van der Hoeven et al 2013[^13] [Netherlands]</td>
<td>Staff patients and visitors to hypertension clinic comparing sequential and simultaneous measures; 132/240 (55%) with hypertension</td>
<td>Mean of three simultaneous repeated measures; Microlife Watch BP® Office</td>
<td>240</td>
<td>11.7% ≥ 10 mmHg \ 5.0% ≥ 15 mmHg \ 1.6% ≥ 20 mmHg</td>
</tr>
<tr>
<td>Canepa et al 2013[^14] [US]</td>
<td>Community sample free of diabetes, stroke, or heart disease at recruitment — the Baltimore Longitudinal Study of Aging</td>
<td>Mean of second and third simultaneous pairs of readings with four-limb device COLIN VP2000</td>
<td>1045</td>
<td>4.8% ≥ 10 mmHg \ 1.1% ≥ 15 mmHg</td>
</tr>
<tr>
<td>Clark et al 2014[^15] [UK]</td>
<td>Community cohorts with and without diabetes recruited to the Diabetes Alliance for Research in England (DARE)</td>
<td>Two Omron HEM 705CP in simultaneous 2 × 2 crossover design; mean of four pairs of readings</td>
<td>514 (diabetes) \ 286 (control)</td>
<td>8.6% ≥ 10 mmHg \ 2.3% ≥ 15 mmHg \ 2.9% ≥ 20 mmHg \ 0.4% ≥ 25 mmHg</td>
</tr>
<tr>
<td>Clark et al 2014[^16] [UK]</td>
<td>Community cohorts with and without diabetes and hypertension</td>
<td>Two Omron HEM 705CP in simultaneous 2 × 3 crossover design; mean of six pairs of readings</td>
<td>265 (diabetes) \ 116 (control)</td>
<td>5.2% ≥ 10 mmHg \ 0.8% ≥ 15 mmHg \ 0% ≥ 20 mmHg \ 5.2% ≥ 10 mmHg \ 2.6% ≥ 15 mmHg \ 0% ≥ 20 mmHg</td>
</tr>
</tbody>
</table>

[^1]: Published and unpublished data; all other studies published data only. ABI = ankle-brachial index.
arm difference ≥10 mmHg were 11.2% (95% confidence interval [CI] = 9.1 to 13.6) for seven populations with hypertension (3858 participants), 7.4% (95% CI = 5.8 to 9.2) for six populations with diabetes (1648 participants), and 3.6% (95% CI = 2.3 to 5.0) for eight community-based groups without diabetes or hypertension (3751 participants) (I² = 76%) was observed across studies in the general population group; there was a lower prevalence for the two cohorts of East Asian origin compared with the six Western groups, which accounted for heterogeneity in the former (2.0% [95% CI = 1.4 to 2.8]; I² = 83%) versus 4.4% (95% CI = 3.5 to 5.5); I² = 14%; P<0.001). Similarly, in the hypertensive population, prevalence was lower in the two East Asian cohorts (8.9% [95% CI = 7.9 to 9.9]; I² = 77%) compared with the remaining Western populations (13.3% [95% CI = 11.0 to 15.7]; I² = 6%; P<0.001 [Appendix 2, available from the authors on request]). The corresponding prevalences for differences ≥15 mmHg were 4.0% (95% CI = 1.9 to 6.8) in hypertension (three cohorts; 2229 participants), 2.3% (95% CI = 1.1 to 3.9) in diabetes (four cohorts; 1165 participants), and 0.7% (95% CI = 0.1 to 1.5) without diabetes or hypertension (five cohorts; 2941 participants; P = 0.004 for subgroup differences). Prevalences were again lower for the one study of a Chinese population compared with the remaining Western cohorts. For differences ≥20 mmHg, prevalences were 1.0% (95% CI = 0.6 to 1.5) (three cohorts; 2229 participants), 0.4% (95% CI = 0 to 1.1) (four cohorts; 1165 participants), and 0.1% (95% CI = 0 to 0.4) (five cohorts; 2323 participants) respectively (P = 0.001); no statistical heterogeneity was observed (Appendix 2, available from the authors on request).

Univariable meta-regression showed two study-level factors to be associated with mean prevalence for systolic inter-arm differences ≥10 mmHg: health status (normotension versus diabetes versus hypertension) and absolute level of systolic blood pressure (Table 2). Each increase of 10 mmHg in absolute systolic blood pressure was associated with a 4% (95% CI = 0.9 to 4.0) increase in prevalence of an inter-arm difference ≥10 mmHg (Figure 3). Mean absolute systolic blood pressure increased across the health status groups (normotension: 128 mmHg [standard deviation (SD) 7.4], diabetes: 139 mmHg [SD 4.2], and hypertension: 148 mmHg [SD 17]; P = 0.02) indicating potential co-linearity of these two variables. Meta-regression of prevalence against health status after adjustment for absolute blood pressure was no longer significant, and no other study-level factors were found to be associated with inter-arm difference prevalence in multivariable analysis (Appendix 2, available from the authors on request).

![Figure 2. Prevalence of systolic inter-arm differences ≥10 mmHg.](image)

![Table 2. Univariable and multivariable meta-regression analyses for systolic inter-arm blood pressure differences ≥10 mmHg](table)
Five studies reported both simultaneously and sequentially measured prevalence data for systolic inter-arm differences ≥10 mmHg. Pooled analysis of data after adjustment for the paired nature of the data gave a prevalence of 6.4% (95% CI = 5.0 to 7.8) for measurement by a simultaneous method compared with 14.6% (95% CI = 12.5 to 16.6; \( P < 0.001 \)) for a sequential method; and a relative risk (RR) for diagnosis of an inter-arm difference by sequential compared with simultaneous measurement of ≥10 mmHg of 2.2 (95% CI = 1.1 to 4.5).

Statistical heterogeneity between studies (I² = 85%) was explained by a single study that reported a higher prevalence of inter-arm differences for simultaneous compared with sequential measurements, whereas all other studies reported lower prevalences for simultaneous measurements. This outlying study result was based on averaging the second and third pairs of readings, but sequentially measured prevalences were higher than simultaneous for each of the three individual pairs of measurements made. Sensitivity analysis by substituting the non-averaged data for this study accounted for the statistical heterogeneity (residual I² = 37%; \( P = 0.17 \)); the resulting RR was 2.9 (95% CI = 2.1 to 4.1).

Visual inspection of funnel plots suggested no publication bias through missing small studies reporting low inter-arm difference prevalences (Figure 4), and the Egger tests were not significant (\( P \)-values = 0.32, 0.26, and 0.75 for inter-arm differences ≥10 mmHg, 15 mmHg, and 20 mmHg respectively (Appendix 2, available from the authors on request).

**DISCUSSION**

**Summary**

This systematic review and meta-analysis presents a contemporary synthesis of estimates of the prevalence of systolic inter-arm differences in populations relevant to primary care. The prevalences of inter-arm difference rise in relation to cardiovascular comorbidity (such as diabetes and/or hypertension) in the population studied for all chosen cut-off values, and comparison with paired sequentially measured differences confirms that prevalence can be overestimated threefold when a simultaneous measurement method is not employed.

**Strengths and limitations**

This study builds on the authors’ previous reviews. The search terms are intentionally broad and therefore it is unlikely that important publications relevant to this review have been missed. The searches were supplemented with an author’s archives, contacts, and peer review activity. This meta-regression demonstrated the univariable association of rising absolute blood pressures and increasing inter-arm difference prevalences. This association did not persist on multivariable regression; however, there was co-linearity of blood pressure with clinical status. Given the relatively small number of included studies, these multivariate meta-regression analyses were potentially underpowered.

**Comparison with existing literature**

The prevalence figures reported here are...
lower than those previously reported in a previous study of hypertension (19.6% ≥10 mmHg [95% CI = 18.0 to 21.3]); however, only four studies met that study’s inclusion criteria in 2006,23,25,44,48 and until recently there was a paucity of data truly representative of general community populations measured by simultaneous methods.4 There has been a rapid expansion of interest in inter-arm difference over the last decade,49 half of the 16 studies contributing to this review were published within the last 4 years,1,6,28,40,43,45 A number were included in the recent review by Singh and colleagues which confirmed that prevalence rates are lower for community-based cohorts compared with hospital data;25 that review reported a community prevalence for systolic differences ≥10 mmHg of 7.5% [95% CI = 5.6 to 9.4]. However, their findings were based on only four cohorts,26,28,42,46 of which one study included 50% subjects with hypertension,26 another reported a mixed population (the lead author of which has provided additional subgroup data for the analyses reported here),28 and the third did not meet the inclusion criteria because it did not report repeated simultaneous measurements.50 Furthermore three studies from the authors’ own research group were misclassified in that review as outpatient studies and excluded from community prevalence analyses, despite correspondence with and provision of additional data to the review’s authors.3,5,6 These factors account for the erroneously high estimate of prevalence for the general population compared with the data presented here. Singh and colleagues also stated that community-based studies included in their review did not report data for systolic inter-arm differences ≥15 mmHg or ≥20 mmHg; data from five such studies are included in this report.4,15,39,40,44

The prevalence of an inter-arm difference in hypertension is higher at any cut-off compared with the non-hypertensive population. Prevalence varies with absolute blood pressure levels.51,52 and these findings of higher prevalences with, rather than without, hypertension are consistent with other reports that did not meet the inclusion criteria for this analysis.2,22,23,25,34 The prevalence figures for diabetes are intermediate between those found for normotensive non-diabetic and hypertensive populations. Inter-arm blood pressure differences are associated with peripheral vascular and cerebrovascular disease,20,35,46 both conditions that share hypertension as a major risk factor.22 It therefore seems plausible that the prevalence of inter-arm differences, which have been described as markers of peripheral arterial disease,10,15,38,39 rise with the baseline vascular risk of the population studied.

This study’s findings suggest that prevalences of an inter-arm difference may vary by ethnicity, with lower prevalences of a ≥10 mmHg difference seen both with and without hypertension for East Asian compared with Western populations. These prevalence differences were not explained by variations in systolic blood pressures between ethnic groups. Recently, in a study designed specifically to compare inter-arm difference between ethnic groups, there were no significant differences in inter-arm prevalences between white British, South Asian, and African Caribbean cohorts.50 However, the larger MESA (MultiEthnic Study of Atherosclerosis) study has reported higher prevalence of systolic inter-arm differences ≥15 mmHg in African American and white non-Hispanic Americans compared with Hispanic or Chinese Americans.51 Few studies have directly compared simultaneous and sequential measurement techniques; the two methods appear to correlate well during a single assessment session,6,42 but not over different visits.7,34 Studies on the reproducibility of an inter-arm difference over time are mainly short term (that is, weeks),6,42 apart from a small 1-year retrospective follow-up in diabetes.7 Prevalence figures have previously been shown to be higher when a sequential rather than a simultaneous measurement technique is employed.3,5,6 Pooled data in this review show a relative risk of detecting a systolic inter-arm difference ≥10 mmHg of 2.9 for sequential compared with simultaneous measurement. A comparable risk ratio (2.2) was reported in a previous systematic review that compared pooled risks across different studies.28 The authors believe that these findings are the first pooled analysis of paired sequential and simultaneous measurements in the same groups of individuals, as opposed to pooled prevalence data derived from unmatched studies according to method of inter-arm measurement.

Prevalence of inter-arm difference declines with number of pairs of measurements,6,42,43,44 possibly in part due to white-coat effects on blood pressure.43,44 Verberk has estimated that an inter-arm difference ≥10 mmHg is twice as likely to be observed when based on a single rather than repeated pairs of simultaneous measurements.28 Recently, devices have
been developed that measure two or four limbs simultaneously. Four studies reporting results from a four-limb device (COLIN VP1000 waveform analyser, Omron, Japan) are included in this analysis.36,38,41,42 Sensitivity analyses for this device did not show different prevalence estimates for any cut-off or subgroup compared to other repeated measurement protocols. It is a sophisticated waveform analysis device and it cannot therefore be assumed that single pairs of measurements obtained by other single or paired devices do not overestimate prevalence. Two studies in this review used a simultaneous two-limb device that averages three pairs of readings [WatchBP® Office, Microlife, UK].37,45 Lohmann and colleagues found no significant differences in prevalence calculated from two or three simultaneous pairs of readings using this device, and there was no evidence of different prevalence findings based on these studies compared with other methods.37

**Implications for research and practice**

Systolic inter-arm differences are associated with higher prevalences of peripheral arterial disease,3,10,20 and with increased cardiovascular and all-cause mortality.19–21 This study’s findings support the current advice in hypertension guidelines that inter-arm difference, when observed, should be confirmed with simultaneous measurement of both arms.26,29 However, detection methods in daily primary care need to be practical or they will not be adopted.46,66 It has been previously found that a single pair of sequential measurements can exclude the presence of an inter-arm difference on simultaneous measurement with good specificity and high negative predictive values (0.97 for ≥10 mmHg and 0.99 for ≥15 mmHg),4 and is associated with increased cardiovascular and all-cause mortality.15 Therefore, a sequential method of measurement still has a role in identifying people in need of further assessment for inter-arm difference. The prevalence figures presented here are useful to estimate how often an inter-arm difference may be missed if not checked for in primary care. For example, with a prevalence of 10%, a systolic blood pressure might be underestimated by ≥10 mmHg through the chance selection of the lower reading arm once in every 20 assessments, leading to false reassurance about, or undertreatment of, high blood pressure.5,10,17,67

This study’s findings quantify the prevalence of inter-arm differences that may be expected in primary care populations, suggesting that an inter-arm blood pressure difference occurs in a significant minority of these patients. Historically, inter-arm difference has not been routinely checked for in primary care,27 although uptake seems to be increasing (CE Clark, unpublished data, 2016) and guideline recommendations are due for review.68 Therefore, practitioners should ensure that a difference has been looked for before making treatment decisions based on blood pressure measurements. A simultaneous method of measurement is needed to confirm the presence of an inter-arm difference and this should be the method of choice for any future studies.

Further work is required to establish the validity of individual devices for accuracy of measurement based on a single pair of measurements, and further data are required to explore more fully any ethnic variations in prevalence or implications of inter-arm differences. The authors are currently conducting an individual patient data meta-analysis that will provide population-specific evidence on prevalence.69

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**Provenance**

Freely submitted; externally peer reviewed.

**Competing interests**

The authors have declared no competing interests.

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## Appendix 1. Search strategy

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<thead>
<tr>
<th>Number</th>
<th>Database</th>
<th>Search term</th>
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<tr>
<td>1</td>
<td>Embase, MEDLINE, CINAHL</td>
<td>(subclavian AND stenosis).af</td>
</tr>
<tr>
<td>2</td>
<td>Embase, MEDLINE, CINAHL</td>
<td>(blood AND pressure AND NEAR AND difference).af</td>
</tr>
<tr>
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<td>(blood AND pressure AND NEAR AND differential).af</td>
</tr>
<tr>
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<td>Embase, MEDLINE, CINAHL</td>
<td>(interarm AND NEAR AND differential).af</td>
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1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9