PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (http://bmjopen.bmj.com/site/about/resources/checklist.pdf) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

This paper was submitted to a another journal from BMJ but declined for publication following peer review. The authors addressed the reviewers’ comments and submitted the revised paper to BMJ Open. The paper was subsequently accepted for publication at BMJ Open.

This paper received three comments on its previous journal but one declined to publish the review alongside with the paper.

ARTICLE DETAILS

<table>
<thead>
<tr>
<th>TITLE (PROVISIONAL)</th>
<th>Which cuff should I use? Indirect blood pressure measurement for the diagnosis of hypertension in obese patients: A diagnostic accuracy review</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUTHORS</td>
<td>Irving, Greg; Holden, John; Stevens, Richard; McManus, Richard</td>
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</tbody>
</table>

VERSION 1 - REVIEW

<table>
<thead>
<tr>
<th>REVIEWER</th>
<th>Teemu Niiranen Framingham Heart Study, Boston University</th>
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<tbody>
<tr>
<td>REVIEW RETURNED</td>
<td>01-Dec-2015</td>
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| GENERAL COMMENTS     | Irving et al. have assessed in a meta-analysis the diagnostic accuracy of different methods of blood pressure measurement compared to reference standards for the diagnosis of hypertension in obese patients with a large arm. The authors conclude that a correctly fitting upper-arm cuff should be used in these patients and if a correctly fitting cuff cannot be applied, measurement at the wrist should be considered.

The research question is relevant, the methods are valid and the question is appropriately answered. The literature review has been thorough and the PRISMA checklist has been filled appropriately. The results of the study show that the sensitivity and specificity of nearly all the methods is actually quite good (>0.85), apart from when an incorrectly fitting cuff is used. >0.85 is quite good because not even two successive measurements performed with the same technique can reach perfect sensitivity and specificity when blood pressure is measured due to the continuously fluctuating nature of blood pressure. The conclusions the authors make based on the data are valid.

However, apart from hypertension experts interested in “finetuning” blood pressure measurement techniques in a subgroup of patients, the article has relatively little interest to the greater public and to the majority of physicians. The guidelines already state that an appropriately sized cuff should be used in everyone, and this is the main message of the article. Patients whose arm is too large even for the largest cuff size are after all quite rare. I think this article should therefore rather be published in a hypertension journal instead of a general medicine journal.

One specific comment: Was invasive blood pressure measured at
the aortic or brachial level in the studies with invasive measurements and would this make any difference in your opinion?

REVIEWER
Christine A’Court
University of Oxford

REVIEW RETURNED
07-Dec-2015

GENERAL COMMENTS
This systematic review is rigorous, relevant, timely and has the potential to alter practice. It provides much needed guidance for clinicians aspiring to diagnose and manage hypertension well in the face of the obesity ‘epidemic’. It addresses the problem encountered increasingly frequently in daily practice—that of the evaluating ‘true’ blood pressure in a person whose arm circumference exceeds the range of readily available upper arm manometer cuffs. Even use of an extra large, so-called thigh cuff is not always possible if the cuff’s vertical dimension is greater than a person’s upper arm’s length. Currently clinicians have to choose between using an inadequate cuff that pops off during inflation unless held together forcefully, a range of alternative methods that lack the endorsement of the usual sources of professional guidance, or to give up on the measurement and simply seek measures of hypertensive end organ damage such as left ventricular hypertrophy or hypertensive retinopathy.

The text, tables 2-3 and figures demonstrate clearly the limitations of available literature, and a rigorous approach to studies retained for analysis. The measured conclusions seem well supported by the data. The table explaining how current recommendations of relevant authorities stand up to the review’s finding is an interesting and unusual inclusion. (nb Typo Table 1, line 18, 2nd column devises/devices) The third and fourth rows (BHS/NICE, and WHO/IHS) have a slightly odd syntax, and the repetitious content of the final cell is disappointing and merits a little editing.

This reviewer works in a practice already equipped with plentiful extra large cuffs, but will now be recommending purchase of a wrist monitor—evidence of the review’s impact, if more evidence is needed.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Comments:
1. Irving et al. have assessed in a meta-analysis the diagnostic accuracy of different methods of blood pressure measurement compared to reference standards for the diagnosis of hypertension in obese patients with a large arm. The authors conclude that a correctly fitting upper-arm cuff should be used in these patients and if a correctly fitting cuff cannot be applied, measurement at the wrist should be considered.

The research question is relevant, the methods are valid and the question is appropriately answered. The literature review has been thorough and the PRISMA checklist has been filled appropriately. The results of the study show that the sensitivity and specificity of nearly all the methods is actually quite good (>0.85), apart from when an incorrectly fitting cuff is used. >0.85 is quite good because not even two successive measurements performed with the same technique can reach perfect sensitivity and
specificity when blood pressure is measured due to the continuously fluctuating nature of blood pressure. The conclusions the authors make based on the data are valid.

Response:
We disagree. This statement fails to acknowledge the relatively poor performance of the other methods such as forearm compared to wrist blood pressure measurement.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Index</th>
<th>No. Studies (No. participants)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive likelihood ratio</th>
<th>Negative likelihood ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correctly fitting cuff</td>
<td>Forearm cuff</td>
<td>6 (425)</td>
<td>0.84</td>
<td>0.75</td>
<td>3.64</td>
<td>0.17</td>
</tr>
<tr>
<td>Correctly fitting cuff</td>
<td>Wrist cuff</td>
<td>5 (217)</td>
<td>0.92</td>
<td>0.92</td>
<td>12.62</td>
<td>0.82</td>
</tr>
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</table>

This comparison is important because guideline developers such as the American Heart Association are currently recommending forearm blood pressure measurement over other methods such as wrist blood pressure measurement. In a general practice population with a large number of patients, forearm blood pressure measurement could be leading to considerable over- and under-diagnosis. Evidence suggests clinicians are currently using a wide variety of methods to diagnose hypertension in obese patients with a large arm circumference. Our findings could help to reduce this variation in practice.

2. However, apart from hypertension experts interested in “finetuning” blood pressure measurement techniques in a subgroup of patients, the article has relatively little interest to the greater public and to the majority of physicians.

Response:
This statement fails to acknowledge the remainder of the main message that if a correctly fitting upper arm cuff cannot be applied or is unavailable then blood pressure measurement at the wrist is sufficiently sensitive and specific to make a diagnosis. This is acknowledged by the second reviewer: “the most important finding is the use of a wrist cuff device when an upper arm BP is not possible in the presence of a very obese arm”. It is established that obese patients experience less discomfort when a cuff is automatically inflated around the wrist than around the upper arm. They are also generally considered easier to use than an upper arm cuffs in obese patients as no undressing is required – an important consideration in 10 minute GP consultations where precise measurement of the upper arm is not practical. This was reflected in the third reviewers comments (a general practitioner): “This reviewer works in a practice already equipped with plentiful extra large cuffs, but will now be recommending purchase of a wrist monitor”. In addition, a large number of patients performing home blood pressure monitoring prefer wrist rather than arm devices, and wrist BP monitors have gained as much as 30% of the market share for all automated BP measuring devices worldwide. Until now, wrist monitors have generally been considered unreliable when compared with traditional measurement at the arm level. Our results provide considerable evidence that wrist monitors are reliable provided they are used properly and the implication of Reviewer 3’s comments are that practice will change in response. We propose to adjust the paper – particularly the introduction and discussion to make these points clearer.

3. The guidelines already state that an appropriately sized cuff should be used in everyone, and this is the main message of the article. Patients whose arm is too large even for the largest cuff size are after all quite rare. I think this article should therefore rather be published in a hypertension journal instead of a general medicine journal.

Response
We disagree: The research question this paper addresses was developed from uncertainties identified in routine general practice in an effort to address an increasingly common problem faced by
GPs. In addition to the UK data quoted above, over 30% of the entire population of the USA have a large arm circumference as a consequence of obesity.9 This figure can rise to over 60% in some clinics.10 In developing countries such as Mexico as many as 42% of the practice population have a large arm circumference.3 The obese patient ‘subgroup’ therefore represents an extremely large number of individuals internationally. The chief source of error in in health care is the quality of the initiating decision and choice of appropriate cuff is an essential prerequisite for an accurate diagnosis of hypertension.11 ‘Miscuffing’ large arms is thought to represent 84% of miscuffings – representing an important source of over diagnosis and under diagnosis.6,12 Given that the consequence of a diagnosis of hypertension is potential life long medication and erroneous exclusion of hypertension places an individual at considerable risk of vascular events and death, patients will be concerned to know that their diagnoses are accurate.13 We propose to adjust the paper – particularly the introduction and discussion to make these points clearer.

4. One specific comment: Was invasive blood pressure measured at the aortic or brachial level in the studies with invasive measurements and would this make any difference in your opinion?

Response:
Invasive blood pressure was measured at the brachial level in all the included studies using this reference standard. No invasive measurement was made at the aortic level and so we are unable to perform a sensitivity analysis to what degree this approach would approach the impact on the relative performance of non-invasive test. Whilst feasible to expect some difference between these two approaches it should be noted that invasive measurement at the brachial artery is a well established approach and widely used method for this reference standard.14,15,16,17,18

Reviewer: 2
Comments:
1. This systematic review is rigorous, relevant, timely and has the potential to alter practice. It provides much needed guidance for clinicians aspiring to diagnose and manage hypertension well in the face of the obesity ‘epidemic’. It addresses the problem encountered increasingly frequently in daily practice that of evaluating ‘true’ blood pressure in a person whose arm circumference exceeds the range of readily available upper arm manometer cuffs.

Response:
We thank the reviewer

2. Even use of an extra large, so-called thigh cuff is not always possible if the cuff’s vertical dimension is greater than a person’s upper arm’s length. Currently clinicians have to choose between using an inadequate cuff that pops off during inflation unless held together forcefully, a range of alternative methods that lack the endorsement of the usual sources of professional guidance, or to give up on the measurement and simply seek measures of hypertensive end organ damage such as left ventricular hypertrophy or hypertensive retinopathy.

Response:
We think that this emphasizes the importance of our paper.

3. The text, tables 2-3 and figures demonstrate clearly the limitations of available literature, and a rigorous approach to studies retained for analysis. The measured conclusions seem well supported by the data. The table explaining how current recommendations of relevant authorities stand up to the review’s finding is an interesting and unusual inclusion. (nb Typo Table 1, line 18, 2nd column devises/devices) The third and fourth rows (BHS/NICE, and WHO/IHS) have a slightly odd syntax, and the repetitious content of the final cell is disappointing and merits a little editing.

Response:
We propose to edit this table along the lines that the reviewer suggests.

4. This reviewer works in a practice already equipped with plentiful extra large cuffs, but will now be recommending purchase of a wrist monitor – evidence of the review’s impact, if more evidence is needed.
Response:
This again supports our contention that this is a real issue for primary care. We have looked at the potential impact in one of our own practices of 4210 patients. 1127 patients (27%) had a BMI >30 and 204 patients (5%) had a BMI >40. A review of the medical records of those with a BMI > 40 revealed at least one failed attempt at upper arm blood pressure measurement in 132 (65%) patients. In the majority of cases no further blood pressure was documented in this high risk group. Some patients declined to have their blood pressure measured because the patient found the need for an extra large cuff ‘embarrassing’. A referral to secondary care for blood pressure measurement was made for 32 patients. In the majority of cases this resulted in 24 hour blood pressure measurement - as our review shows, there is insufficient evidence for this test in obese patients with a large arm circumference. We believe that this data from everyday practice supports our contention that measurement of obesity is not simply an issue for “hypertensionologists”.

References
## VERSION 2 – REVIEW

<table>
<thead>
<tr>
<th>REVIEWER</th>
<th>Dr Victoria Allgar</th>
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<tbody>
<tr>
<td></td>
<td>University of York</td>
</tr>
<tr>
<td>REVIEW RETURNED</td>
<td>09-Jun-2016</td>
</tr>
</tbody>
</table>

### GENERAL COMMENTS

Overall a clearly written paper utilising the correct statistical analysis.