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Design and evaluation of a low-cost sphygmomanometer to monitor women with pre-eclampsia in low-resource settings

Laura Causey,[a] Sam Meja,[b,c] Edward Cleo Kommwa,[b,c] Phylos Bonognwe,[b,c,d] Ron Mataya,[b,c,e] Ha Nguyen,[f] Hector Mendez-Figueroa,[f] Erica Skerrett,[a] Tyler Young,[a] Kelley Maynard,[a] Z. Maria Oden,[a,g] Rebecca Richards-Kortum[a,g*]

[a] Rice 360: Institute for Global Health, Rice University, Houston, Texas, USA
[b] Department of Obstetrics and Gynecology, Queen Elizabeth Central Hospital, Blantyre, Malawi
[c] Department of Obstetrics and Gynecology, University of Malawi College of Medicine, Blantyre, Malawi
[d] National Committee on Confidential Enquiry into Maternal Death, Malawi
[e] School of Public Health, Loma Linda University, Loma Linda, California, USA
[f] Department of Obstetrics, Gynecology and Reproductive Sciences, The University of Texas Health Science Center at Houston, Houston, Texas, USA
[g] Department of Bioengineering, Rice University, Houston, Texas, USA

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Abstract

We developed and pilot tested a sphygmomanometer designed to monitor pregnant women in low-resource settings. Blood pressure was assessed in 138 subjects, including healthy adults (n=85), pregnant women (n=42), and women at-risk for pre-eclampsia (n=11) using the novel sphygmomanometer, manual auscultation, and the GE Dinamap Procare 400. Accuracy of the device was evaluated by comparing measurements of the test device and the Dinamap in healthy volunteers and pregnant women in Texas and in women at risk for pre-eclampsia in Malawi. Measurements from the test device in pregnant and healthy volunteer populations differed from those collected using the auscultatory method by 0.2 mmHg (95% CI: -18.8 to 19.2, systolic) and -2.8 mmHg (95% CI: -21.0 to 15.4, diastolic). In women at risk for pre-eclampsia, measurements with the test device differed from those of the Dinamap on average by 2.9 mmHg (95% CI: -29.3 to 35.1, systolic) and -5.4 mmHg (95% CI: -45.8 to 34.9, diastolic). Compared against the auscultatory method, measurements with the Dinamap differed on average by 0.0 mmHg (95% CI: -31.8 to 31.9, systolic) and -3.7 mmHg (95% CI: -28.6 to 21.3, diastolic). Accuracy was reduced when patients were moving or not seated during measurement. When testing the device against British Hypertension Society standards, the device achieved a grade of A/A in pregnant persons. This sphygmomanometer has the potential to provide low-resource hospitals with an affordable, accurate option for regular blood pressure monitoring. However, algorithm improvements are needed to reduce sensitivity to subject motion and posture.

Keywords: blood pressure monitor; pregnancy; low-resource settings; medical device; design

Introduction

Globally, 14-18.5% of maternal deaths are related to hypertensive disorders during pregnancy, including pre-eclampsia and eclampsia (Bhutta and Black, 2013; WHO, 2016; National Committee on Confidential Inquiries into Maternal Deaths, 2018). Pre-eclampsia is usually indicated by new-onset elevated blood pressures (>140 mmHg systolic or >90 mmHg diastolic) and proteinuria levels (>0.3 g) after 20 weeks of pregnancy

* Corresponding author: rkortum@rice.edu

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(ACOG, 2002). Women with pre-eclampsia are at risk for eclampsia, characterized by the onset of life-threatening convulsions. Although the etiology of pre-eclampsia is unknown, treatment with magnesium sulfate ($MgSO_4$) and antihypertensive medications has been shown to prevent the onset of eclamptic convulsions and reduce the risk of death due to pre-eclampsia by over 50% (EngenderHealth, 2007; Say et al., 2014).

Women in developing countries are seven times more likely to develop pre-eclampsia, three times more likely to have the disease progress into eclampsia, and then up to 14 times more likely to die from eclampsia than their counterparts in developed countries (EngenderHealth, 2007). To address these disparities, new standards have been implemented to reduce barriers to $MgSO_4$ treatment in low-resource settings. These efforts include developing $MgSO_4$ "treatment packs" and incorporating $MgSO_4$ treatment into national health guidelines (EngenderHealth, 2007), researching the effectiveness of a simplified $MgSO_4$ administration regimen (Begum, Begum, and Quadir, 2002), and designing appropriate, low-cost devices for accurate intravenous infusion of $MgSO_4$ (Juarez, et al., 2016; Mundle, et al., 2012).

Despite these efforts, identification and proper monitoring of women suffering from pre-eclampsia in low-resource settings remains hindered by a lack of appropriate commercial blood pressure monitoring devices . While the auscultatory technique to measure systolic and diastolic blood pressure is relatively inexpensive and is considered the gold standard when used properly (Parati, et al., 2005), the shortage of nurses, the need for extensive training, ambient noise, and common rounding errors prevent the technique from being accurately employed in crowded, under-staffed hospitals in low-resource settings. The World Health Organization (WHO) therefore recommends the use of automated blood pressure monitors in low-resource settings, but only if they are "validated and affordable" (Parati, et al., 2005). In summary, the blood pressure (BP) monitor required by district and referral government hospitals in low human development index countries must be (1) low-cost, (2) automatic, (3) rechargeable battery-powered, (4) validated on pregnant persons with pre-eclampsia and eclampsia, and (5) coupled with appropriate alarm settings.

Currently, there are no automated BP devices designed to monitor automatically at regular intervals that are both low-cost and validated in pre-eclamptic and eclamptic women . Automated, noninvasive blood pressure measurement devices utilize an oscillometric technique—simply put, they analyze the pulsatile oscillations apparent in the increasing or decreasing cuff pressure to calculate systolic and diastolic blood pressures based on proprietary algorithms (Babbs, 2012). The algorithms in most commercial monitors are not designed using data obtained from pregnant women or pre-eclamptic and eclamptic populations, which is of clinical concern as pregnancy-associated arterial compliance can affect the accuracy of such empirical algorithms in ways that are not well understood (Amoore, 2006). The Microlife BP 3AS1-2 Blood Pressure Monitor was found accurate in a study of 45 pregnant women of whom 15 had pre-eclampsia. The Microlife requires manual inflation, restricting its benefit in understaffed wards where at-risk women require regular BP monitoring (Nathan, et al., 2015). Another blood pressure monitor validated in pre-eclamptic and eclamptic populations, the GE Dinamap ProCare 400 Monitor (De Greeff, et al., 2010), collects regular BP readings but costs upwards of $1000. Other low-cost monitors exist (i.e. Omron brand, Homedics brand), but typically are not suitable for one or more of the following reasons: 1) marketed for home use (i.e. Homedics brand); 2) not validated on pregnant women or women with pre-eclampsia and eclampsia; 3) not automatic (Ngene and Moodley, 2019).

These limitations highlight the pressing need of maternal healthcare providers in resource-limited settings who require a fully automatic, regular blood pressure monitor that is optimized for accuracy among pre-eclamptic and eclamptic women, is low-cost and easy to operate, and does not rely on a stable source of electricity. In this paper, we describe the design of an automated sphygmomanometer to address the shortcomings of existing blood pressure monitors and report its accuracy calculating systolic and diastolic blood pressures during pilot studies in (1) healthy adults, (2) pregnant women, and (3) women at risk for or diagnosed with pre-eclampsia in a low-resource maternity ward.

Materials and methods

Our prototype device was created to be a low-cost solution to accurately measure blood pressure in clinical settings where pregnant women, particularly those with pre-eclampsia, require monitoring at regular intervals. The device was designed to meet the following constraints: (i) is accurate for pregnant and non-pregnant subjects (O'Brien, et al., 1993), (ii) has ambulatory capabilities, (iii) has the capability to notify the clinician

when blood pressure exceeds or drops below preset thresholds, (iv) is affordable in low-resource settings, and (v) is easy for nurses in low resource settings to use.

Hardware

Figure 1(A) shows a photograph of the device in use. The main components of the device include a cuff, a pump to inflate the cuff, passive and solenoid valves to control cuff inflation and deflation, a pressure sensor (Omron 2SMPP-02) and instrumentation amplifier (Texas Instruments INA 333) to measure the oscillometric pressure wave during cuff deflation, a microcontroller (Texas Instruments C2000 F28069M) to control the system and process data, as well as LEDs and an LCD display (Nokia 5110) to show the results.

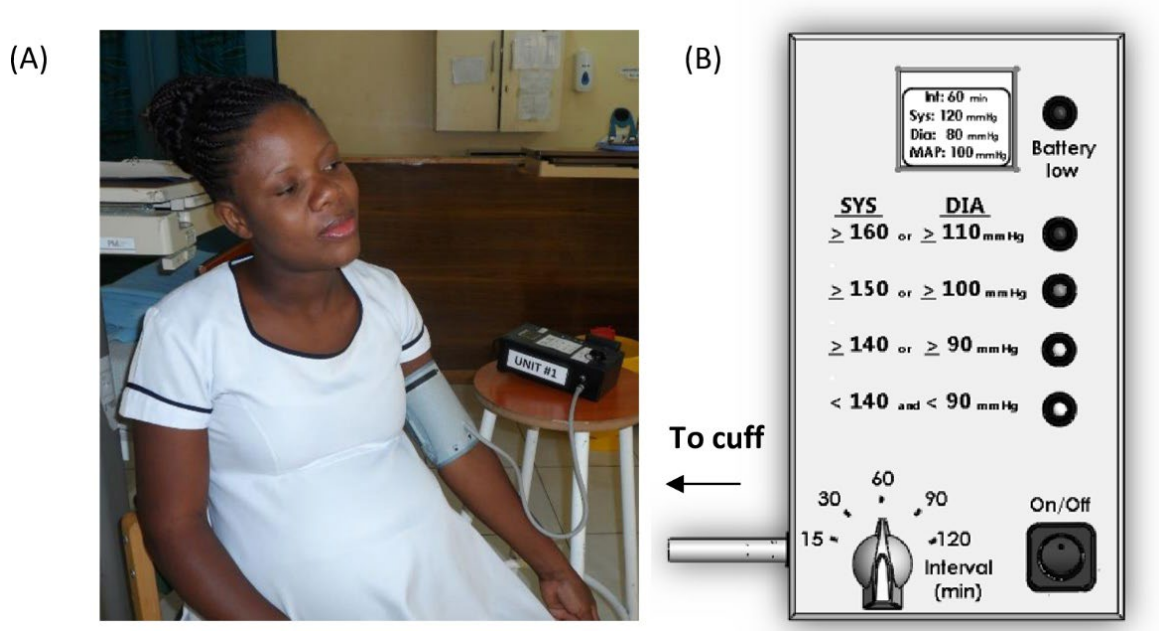

Figure 1: (A) Low-cost blood pressure monitor in use; (B) diagram of user interface. (The participant in the photograph gave permission for the photograph to be published.)

User interface

The user interface, shown schematically in Figure 1(B), includes an On/Off switch, a switch to set the time interval between measurements, a low battery indicator, and a LCD that displays the systolic, diastolic, and mean arterial pressures and the current interval between blood pressure measurements. Warning LEDs indicate when the most recent blood pressure reading exceeds preset levels (from most to least severe): (i) systolic $\geq$ 160 or diastolic $\geq$ 110, (ii) systolic $\geq$ 150 or diastolic $\geq$ 100, (iii) systolic $\geq$ 140 or diastolic $\geq$ 90, and (iv) systolic $<$ 140 and diastolic $<$ 90.

Software

At each measurement interval, the cuff is initially inflated to a pressure of 180 mmHg; the passive valve then releases pressure. As the cuff deflates, the pressure is recorded over time at a sampling rate of 32 Hz. The device is programmed so that if a maximum peak is not found the device reinflates to a pressure of 240 mmHg. If the maximum peak is not found after the second attempt, the LCD displays an error message.

Figure 2(A) shows a typical example of the resulting pressure vs time signal. To calculate mean arterial, systolic and diastolic pressures, the pressure vs time signal is first fit to an exponential decay using least squares. The residual difference between the measured signal and the exponential fit is then filtered using a 2nd order Butterworth bandpass filter with normalized high and low cutoff frequencies of 0.02 Hz and 0.21 Hz, respectively, to further reduce noise. A typical example of the smoothed oscillometric pulse signal is shown in Figure 2(B).

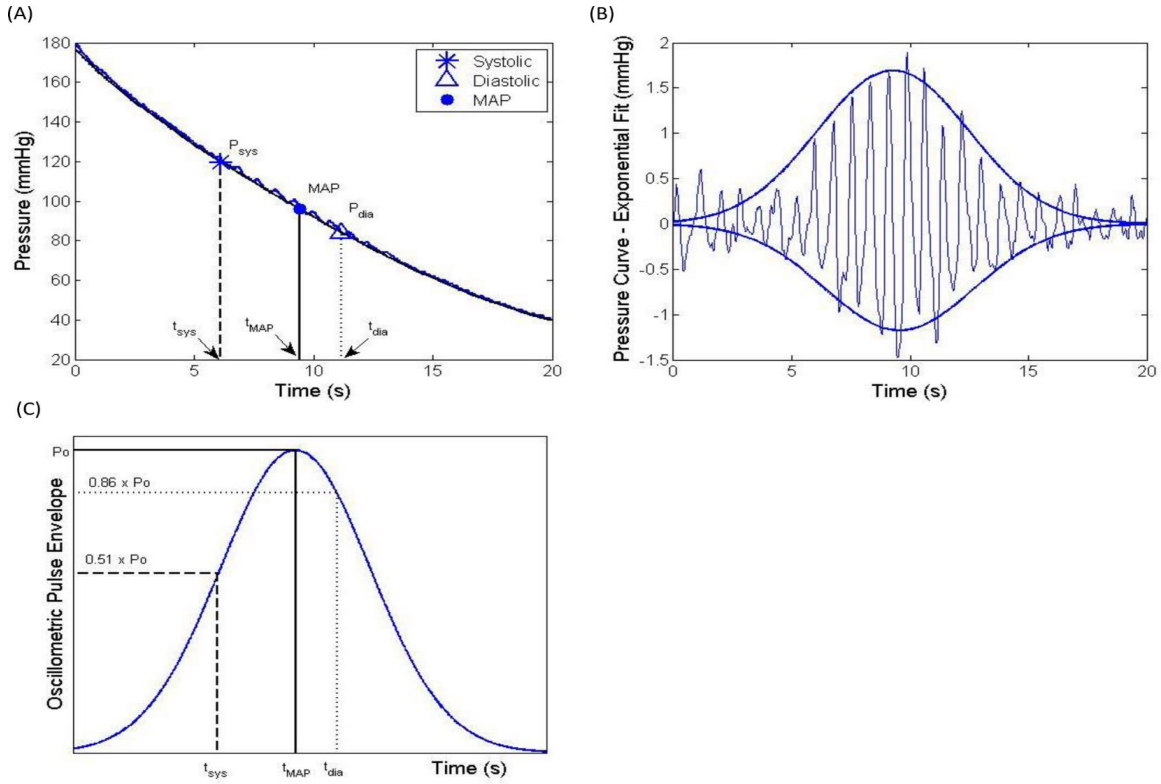

Figure 2: (A) Pressure vs. time measured during cuff deflation is fit to an exponential curve. (B) The envelope of the oscillometric pulse signal is fit to Equations. 1-2. (C) The oscillometric pulse envelope is used to identify the times at which the systolic, diastolic, and mean arterial pressures occur.

Maxima and minima are identified in the oscillometric pulse signal and the envelope corresponding to maxima is fit to Equations 1-2:

$$P_{env}(t) = P_o \exp\left(-\left(t - t_{MAP}\right)^2 / t_1^2\right) \qquad \text{if} \qquad t \le t_{MAP} \tag{1}$$

$$P_{env}(t) = P_o \exp\left(-\left(t - t_{MAP}\right)^2 / t_2^2\right) \qquad \text{if} \qquad t \ge t_{MAP} \tag{2}$$

where t_{MAP} is the maximum peak location, P_o is the peak amplitude, t_1 is the width of the pressure envelope on the left side of the maximum peak, and t_2 is the width of the pressure envelope on the right side of the maximum peak. Gauss-Newton Equations are iterated 60 times to achieve a fit. Similarly, the envelope corresponding to the absolute values of the minima is fit independently to Equations 1-2. The positive oscillometric pulse envelope is calculated as the difference between the top and bottom pressure envelopes fit to minima and maxima and is represented by Equation 3:

$$P_{env,tot}(t) = P_{env,top}(t) - P_{env,bottom}(t) \tag{3}$$

As shown in Fig. 2(C), there are three points of importance on the oscillometric pulse envelope: (1) the peak, P_o, and the corresponding time at which the pressure sensor records the mean arterial pressure (t_{MAP}), (2) the systolic amplitude, r_s x P_o, and the corresponding time at which the pressure sensor records the systolic pressure (t_{sys}); and (3) the diastolic amplitude, r_d x P_o, and the corresponding time at which the pressure sensor pressure sensor records the diastolic pressure (t_{dia}). Typically, the systolic and diastolic amplitudes are expressed as a fraction of the peak amplitude, where r_s and r_d represent the systolic and diastolic fractions, respectively. For example, other studies have reported the systolic fraction ranging from 0.45 - 0.73 and the diastolic fraction ranging from 0.69 - 0.83 (Forouzanfar, et al., 2015; Amoore, 2012). Here, these values were determined from clinical studies with pregnant patients as described below. Once the peak, the systolic amplitude and diastolic amplitude and their corresponding times have been identified on the oscillometric pulse envelope (Figure 2(C)),

the corresponding mean arterial, systolic and diastolic pressures can be determined from the pressure vs time signal (Figure 2(A)). The mean arterial pressure is the pressure measured at the time corresponding to the peak in the pressure envelope; the systolic and diastolic pressures are those measured at the time corresponding to the systolic and diastolic amplitudes.

Ethics statement

The device was evaluated in three single-arm clinical studies targeting three different subject populations: 1) pregnant women attending a routine prenatal clinic at the University of Texas Health Science Center; 2) healthy volunteers attending community health fairs in Houston, Texas; and 3) women at risk for pre-eclampsia or already diagnosed with pre-eclampsia at the maternity ward at the Queen Elizabeth Central Hospital in Blantyre, Malawi. The pregnancy study (NCT02319174), healthy adult study (NCT02267577), and pre-eclampsia study (NCT02258256) were each registered with ClinicalTrials.gov. All study protocols were reviewed and approved by the Institutional Review Board at Rice University (14-082F). The protocols were also reviewed and approved at the institution where subject recruitment took place, including the IRB at the University of Texas Health Science Center at Houston (HSC-MS-14-0273) and the University of Malawi College of Medicine Research and Ethics Committee (P.04/14/1548). The studies took place during January-November of 2015. Written informed consent was obtained from subjects before they were enrolled in the study. Sample sizes were chosen based on recommendations for validation and special group validation in British Hypertension Society (BHS) guidelines (O'Brien et al., 1993). Once goal sample sizes were reached, the study was complete.

Pregnancy study

The system was evaluated in a high resource setting in a population of pregnant women during routine visits at a prenatal clinic. Subjects were eligible if they were at least 20 weeks pregnant and over the age of 18 years. Testing was done in accordance with BHS guidelines (BHS, n.d.; O'Brien et al., 1993). Subjects were seated in a quiet room in an upright comfortable chair with arm at heart level. A blood pressure cuff was placed on the subject's arm; proper cuff sizing was verified by measuring the arm circumference. Blood pressure was measured using the test device as well as using the auscultatory method with a mercury sphygmomanometer; blood pressure was measured a total of nine times, alternating between the test device and the auscultatory method (gold standard). Within ~60 s of the gold standard measurement, the test device was used to take a measurement on the same arm of the subject. Measurements were taken by observers who had completed training materials available on the BHS website and had experience taking blood pressure measurements (BHS, 2016; O'Brien et al., 1993). Two observers separated by a partition took independent simultaneous gold standard measurements by simultaneously listening to the Korotkoff sounds using a dual headed stethoscope.

The pressure/voltage data were recorded using the test device. Data from every other subject was used as a training set to develop an algorithm to calculate the systolic and diastolic coefficients to maximize agreement between the blood pressure measured by the device and the auscultatory gold standard. Accuracy of the device was then assessed using the other half of the data analyzed with the coefficients developed in the training set. Results were compared to the gold standard.

Data from subjects were excluded from further analysis if observers noted movement or had difficulty hearing Korotkoff sounds. The data were analyzed as referenced in the BHS guidelines (O'Brien et al. 1993), which include discarding the first two measurements, selecting the gold standard data from the observer whose readings are more favorable to (closer to) the test device for analysis, and selecting the gold standard values taken before the test measurement or afterwards, depending on favorability to the test device. The BHS accuracy criterion between observers required 80% of differences between the two observers' readings to be within 5 mmHg and 95% within 10 mmHg.

Healthy volunteer study

The system was evaluated in a population of healthy volunteers attending community health fairs in Houston, Texas; subjects were eligible if they were over the age of 18 years. The procedure above was repeated and

results were analyzed using the algorithm developed in the pregnancy study and compared to the auscultatory gold standard.

Pre-eclampsia study

The system was evaluated in a low-resource setting in a population of women who were determined by clinical staff to be at risk for pre-eclampsia or already diagnosed with pre-eclampsia. Subjects were recruited from the maternity ward at the Queen Elizabeth Central Hospital in Blantyre, Malawi, and were eligible if they were over the age of 18 and either pregnant or up to 48 hours postpartum and clinically identified to benefit from regular blood pressure monitoring.

Proper cuff sizing was verified by measuring the subjects' arm circumferences. Patients were situated on cots in a busy maternity ward in a comfortable posture. Subjects wore blood pressure cuffs on each arm for a period of 24-48 hours. One cuff was attached to the test device and the other to a calibrated GE Dinamap ProCare 400 Monitor (Dinamap), the gold standard commercial device for continuous blood pressure monitoring of pregnant women. The test device and Dinamap blood pressure measurements were simultaneously recorded by a trained observer for time intervals between 15 min and 60 min, depending on the needs of the subject. In addition, a nurse recorded the systolic and diastolic blood pressure using the auscultatory method. Although BHS guidelines recommend a mercury sphygmomanometer, due to equipment availability, nurses used an aneroid gauge sphygmomanometer and stethoscope (manual) every 60 min on the same arm as the test device within 1 min of the test device reading. Data were analyzed as described above for the entire group as well as for the subgroup of patients who were seated and did not move during measurement according to observers' notes.

Results

Demographics for subjects participating in the three trials prior to any exclusions are shown in Table 1. Eighty-five subjects were recruited from the campus at Rice University and forty-two subjects were recruited from the University of Houston Obstetrics and Gynecology clinic for the healthy volunteer study and pregnancy study, respectively.

Table 1: Demographics

Subject demographics	Healthy volunteer study	Pregnancy study	Pre-eclampsia study
Number of subjects	85	42	11
Number of test device measurements	255	126	462 (Dinamap) 462 (test device) 426 (manual)
Subjects pre-delivery	N/A	42	6
Subjects post-delivery	N/A	0	5
Male	23.5 %	0 %	0 %
Female	76.5 %	100 %	100 %
Median age (range)	50 yr (18-70)	29 yr (18-43)	28 yr (20-38)
Median arm circumference (range)	30 cm (23-42)	30 cm (24-49)	29 cm (25-34.5)
Median gestational age (range)	N/A	33 wks (22-42)	35 wks (16-41)
Median hours since delivery (range)	N/A	N/A	5 hr (1.5-8)

Data from two subjects in the healthy volunteer study were excluded after the observers stopped the study because the subjects reported symptoms of illness. Data from another two subjects in the healthy volunteer study were excluded because the solenoid valve released too early to collect pressure/voltage data. Data from another nine subjects in the healthy volunteer study were excluded because the observer noted subject movement or reported difficulty in hearing Korotkoff sounds. One subject in the pregnancy study left prior to completing all measurements; data from another five subjects were excluded on account of the observer noting subject movement or difficulty in hearing Korotkoff sounds. Data from the pre-eclampsia study were analyzed

including a subset of data from the subjects who were in a seated posture and not moving during measurement as well as for all subjects, regardless of posture or movement. A CONSORT flowchart is provided in Figure 3.

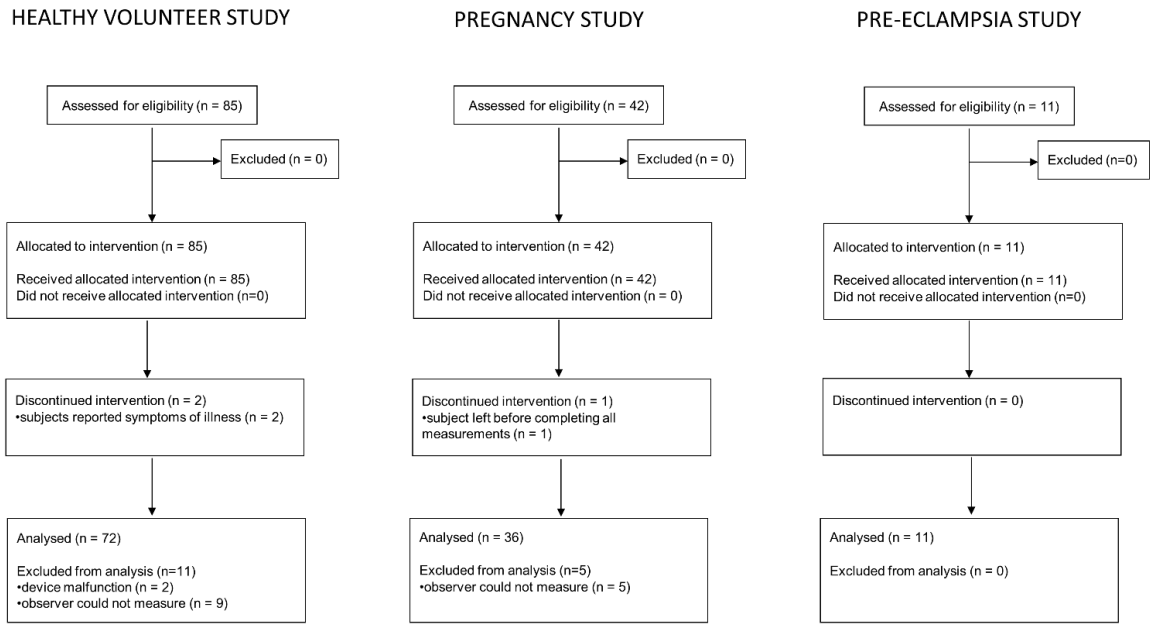

Figure 3: CONSORT flow diagram

Using the training set data from the pregnancy study, the systolic and diastolic coefficients were determined to be $r_{sys} = 0.51$ and $r_{dia} = 0.86$. These values were used to calculate systolic and diastolic pressures in all other subjects.

For the healthy volunteer study, 97% and 100% of differences between the two observers' readings were within 5 mmHg and 10 mmHg, respectively, and 92% and 100% of differences between the two observers' readings were within 5 mmHg and 10 mmHg, respectively, for the pregnancy study. The percentage of subjects in each blood pressure range as measured by the gold standard or the manual method (in the case of the preeclampsia study) is shown in Table 2.

Table 2: Blood pressure distribution

Blood pressure (mmHg)		**Percentage in category**		
		Healthy volunteer study (n = 85)	**Pregnancy study (n = 42)**	**Pre-eclampsia study (n = 11)**
Systolic	**< 90**	1 %	0 %	5 %
	90 - 129	69 %	83 %	32 %
	130 - 160	26 %	17 %	49 %
	161 - 180	3 %	0 %	14 %
	> 180	0 %	0 %	1 %
Diastolic	**< 60**	19 %	28 %	10 %
	60 - 79	47 %	61 %	32 %
	80 - 100	33 %	11 %	48 %
	101 - 110	0 %	0 %	8 %
	> 110	0 %	0 %	2 %

Test device measurements were evaluated according to validation tests outlined by the BHS, although lower recruitment numbers and blood pressure distributions prevented the device from receiving letter grades according to the criterion in the BHS Standards; if assigned, the device would receive a grade of B/A for the healthy volunteer study and a grade of A/A for the pregnancy study (O'Brien et al. 1993). Table 3 shows the

cumulative percentage of readings that have an absolute difference between the more favorable observer's mercury sphygmomanometer readings and the test device of < 5 mmHg, < 10 mmHg, and < 15 mmHg.

Table 3: Test Device Validation

		Absolute difference between standard and test device (mmHg)			Grade
		<5	<10	<15	
		Cumulative percentage of readings			
Healthy Volunteer Study	**SYS**	56%	79%	92%	B
	DIA	53%	77%	90%	B
Pregnancy Study	**SYS**	67%	85%	98%	A
	DIA	70%	89%	98%	A
Healthy Volunteer + Pregnancy Study	**SYS**	59%	80%	93%	B
	DIA	56%	80%	92%	B

Figure 4 shows Bland-Altman plots comparing systolic and diastolic pressures measured with the test device to the gold standard for the healthy volunteer study and validation data in the pregnancy study. For the combined studies, the mean systolic pressure differed by 0.2 mmHg (95% limits of agreement: -18.8 to 19.2 mmHg), while the mean diastolic pressure differed by -2.8 mmHg (95% limits of agreement: -21.0 to 15.4 mmHg). Overall, agreement was better in the validation subset of the pregnancy study, where the mean difference observed in systolic pressure was 1.1 mmHg (95% limits of agreement: -17.0 to 19.1 mmHg) and for diastolic pressure was 0.7 mmHg (95% limits of agreement -16.5 to 17.8 mmHg).

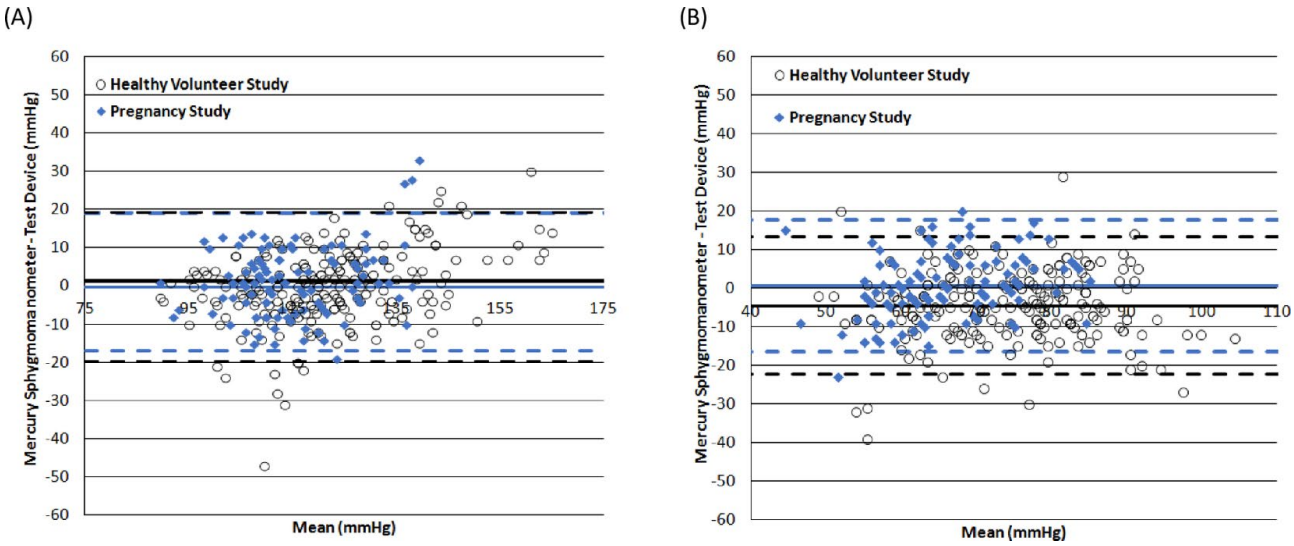

Figure 4: Bland-Altman plots for (A) systolic pressure and (B) diastolic pressure measured in the healthy volunteer study and in the validation subset of the pregnancy study. The solid line indicates the mean difference between the test device and the gold standard (auscultatory method with mercury sphygmomanometer) and the dashed lines show the 95% limits of agreement.

Figure 5 shows Bland-Altman plots comparing the measurements made with the Dinamap to that of the test device as well as to the manual measurements taken during the pre-eclampsia study for subjects who were seated and not moving at the time of measurement. Compared to the Dinamap, the systolic pressure measured with the test device had mean differences of 2.9 mmHg (95% limits of agreement: -29.3 to 35.1 mmHg) and diastolic pressure had a mean difference of -5.4 mmHg (95% limits of agreement: -45.8 to 34.9 mmHg). Interestingly, the Bland-Altman plot comparing the Dinamap and the manual gold standard data shows similar differences; the mean difference in systolic pressure was 0.0 mmHg (95% limits of agreement: -31.8 to 31.9 mmHg) and the mean difference in diastolic pressure was -3.7 mmHg (95% limits of agreement: -28.6 to 21.3 mmHg).

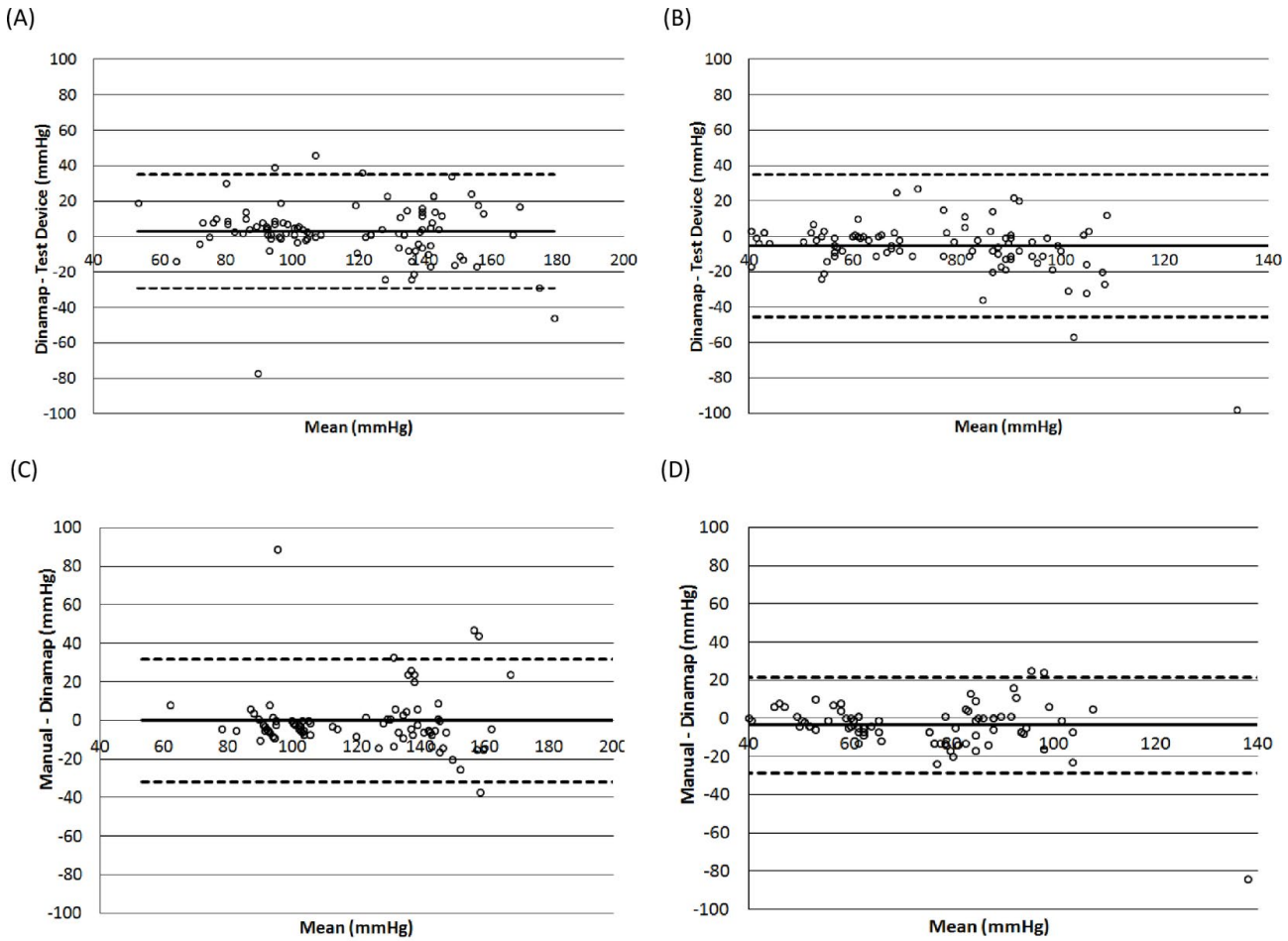

Figure 5. Bland-Altman plots for the pre-eclampsia study using data from subjects that were seated and quiet. Plots compare: (A) the systolic pressure and (B) the diastolic pressure measured with the test device and the Dinamap; and (C) the systolic pressure and (D) the diastolic pressure measured with the Dinamap and the manual gold standard. The solid line indicates the mean of the differences and the dashed lines show the 95% limits of agreement.

Figure 6 shows Bland Altman plots that include all data acquired in the pre-eclampsia study. For 73% of measurements, subjects were lying down and not moving. Subjects were noted to be moving during 4% of measurements. Postural changes and movement reduced agreement with the gold standard for the test device, while results measured with the Dinamap were less sensitive to these changes. The systolic pressure measured with the test device had a mean difference of 2.0 mmHg (95% limits of agreement: -50.6 to 54.7 mmHg) and the diastolic pressure had a mean difference of -9.9 mmHg (95% limits of agreement: -63.5 to 43.7 mmHg) when compared to the Dinamap. Compared to the manual gold standard data, the Dinamap measurements had a mean difference in systolic pressure of 2.1 mmHg (95% limits of agreement: -29.9 to 34.1 mmHg) and a mean difference in diastolic pressure of 0.2 mmHg (95% limits of agreement: -21.1 to 21.5 mmHg).

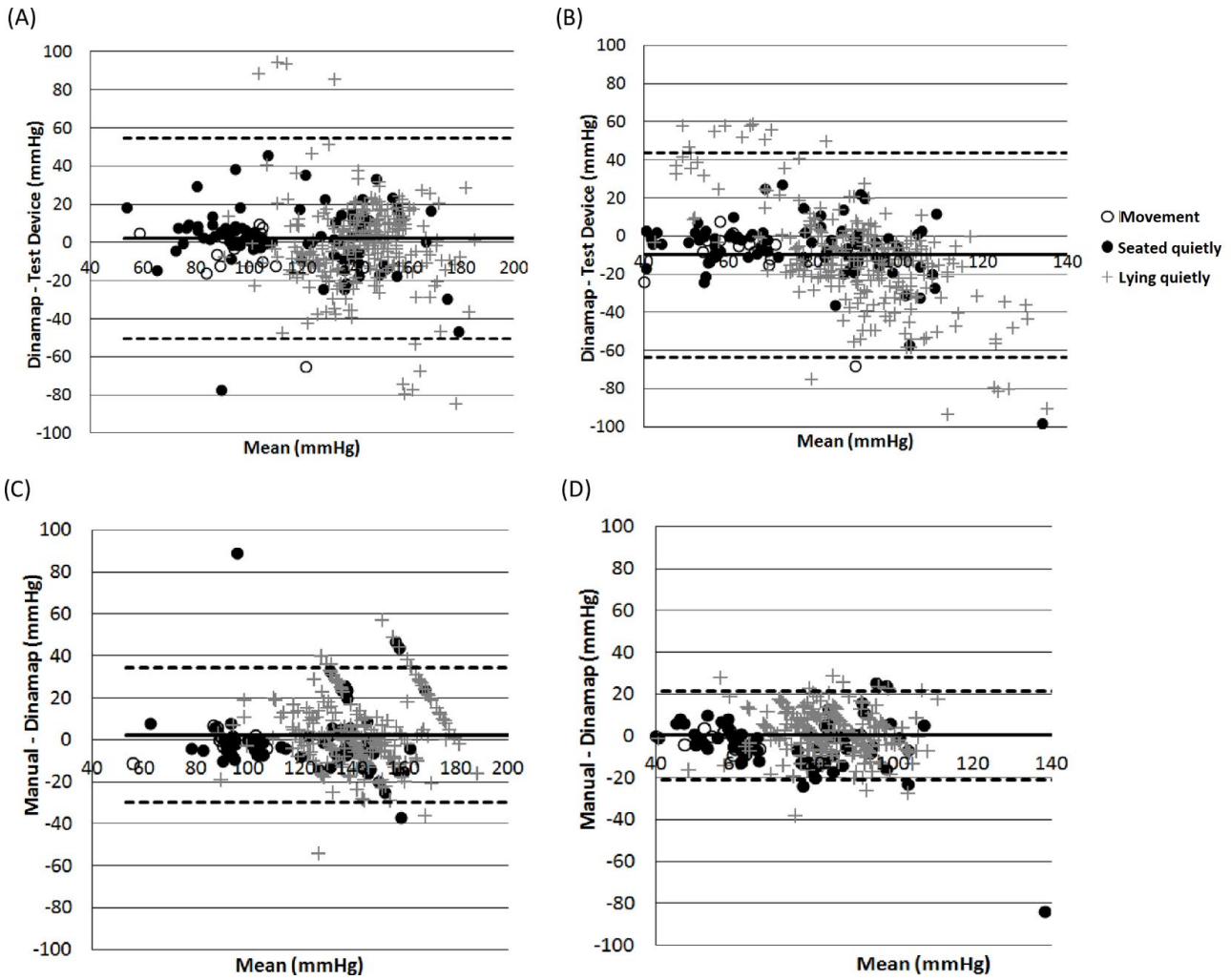

Figure 6: Bland-Altman plots for the pre-eclampsia study with no exclusions noting the subjects' posture and whether they were moving at the time of measurement. Plots compare: (A) the systolic pressure and (B) the diastolic pressure measured with the test device and the Dinamap; and (C) the systolic pressure and (D) the diastolic pressure measured with the Dinamap and the manual gold standard. The solid lines indicate the mean difference and the dashed lines show the 95% limits of agreement.

Discussion

Here, we report a new automated oscillatory sphygmomanometer designed to identify and monitor women with pre-eclampsia and eclampsia in low-resource settings. The device was evaluated to automatically measure blood pressure at regular intervals and alarm when values exceed or drop below a variable, pre-set threshold. At low volume, the cost of goods to manufacture the battery-powered sphygmomanometer was $125. Nurses working in a maternity ward at a large central hospital in sub-Saharan Africa were able to properly use the device with 90 minutes of training.

We tested the accuracy of the device in clinical trials targeting three different subject populations: 1) healthy volunteers; 2) pregnant women; and 3) women at risk for pre-eclampsia or already diagnosed with pre-eclampsia. Compared against the auscultatory gold standard, BP measurements with the test device differed by less than 15 mmHg for 90% - 92% and for 98% of populations of healthy volunteers and pregnant women, respectively, in these studies.

In addition to evaluating performance in a controlled setting under the guidelines for collection methods outlined in the BHS protocol for blood pressure measuring devices (O'Brien et al. 1993), the test device was evaluated in its intended setting; the pre-eclampsia study took place in the maternity ward at the Queen Elizabeth Central Hospital and was used by nurses routinely working in the ward. Under these conditions, subjects who were quietly seated upright did not have the proper arm rest recommended in the BHS protocol and environmental noise

during auscultatory readings may have influenced the observers' results. Based on study equipment availability, the observers were provided with a gauge sphygmomanometer rather than a mercury sphygmomanometer. Aneroid gauge sphygmomanometers are considered an acceptable alternative due to concerns surrounding mercury toxicity (Ngene and Moodley, 2018; Ngene and Moodley, 2019). Additionally, there was only one observer taking a gold standard measurement, preventing observer comparison in cases in which human error was suspected. The BHS protocol requires that the data be analyzed by selecting the gold standard systolic and diastolic values of each subject that are more favorable to the test device (O'Brien et al. 1993). Under the conditions described above, measurements with the test device on average agreed within 6 mmHg with results measured using a commercial Dinamap ProCare Monitor, but the 95% limits of confidence ranged from ±30 to 45 mmHg. The large limits of agreement are common to oscillometric BP monitors; oscillometric ratios can be influenced by arterial stiffness and other variables. Other methods, such as combining Korotkoff sounds with the oscillometric method, may provide additional accuracy. Interestingly, under the same conditions, results measured with the Dinamap ProCare Monitor agreed on average within 4 mmHg compared to auscultatory measurements and the 95% confidence intervals approached ±30 mmHg. Furthermore, results measured with the test device, and to a lesser extent the Dinamap ProCare, were found to be sensitive to changes in both subject posture and movement, reducing agreement with the manual gold standard.

There is an important global need for affordable, appropriate tools to accurately identify and monitor women at risk for pre-eclampsia in low-resource settings. This study presents a novel automated sphygmomanometer designed to meet this need. Strengths of the study include evaluation of the performance of the device both in a controlled environment outlined by the BHS and in a low-resource setting by the intended users. Despite harsh environmental conditions at the Queen Elizabeth Central Hospital, including power outages, high temperature and humidity, the device experienced no technical failures. Users noted ease of use including the simple power and alarm interval switches, helpful LED indicators, and ease of automated measurement. Nurses required less instruction when operating the test device as compared with the Dinamap, including powering on/off the device and setting/changing the timed interval. The usability of the test device can be attributed to the simplicity of its design as compared with the Dinamap.

A limitation of the study is the small sample size and the relatively small number of subjects with hypo- and hypertension. The BHS guidelines recommend that a device be tested on eighty-five subjects. However, data from several of our 85 subjects were excluded during our healthy volunteer study, and we did not enroll the recommended number of subjects for each blood pressure category. For example, the BHS recommends that at least 8 subjects have systolic and diastolic pressures of >180 mmHg and >110 mmHg, respectively. For a device to be validated for pregnant women, the BHS recommends that 30 subjects be tested and that of those at least five have systolic and diastolic blood pressures of 146-160 mmHg and 91-105 mmHg, respectively. No guidelines for pre-eclamptic subjects have been provided by the BHS. Although the pre-eclampsia/eclampsia study presented here was a small pilot study, it demonstrated that this device was feasible for use in low-resource settings. However, the BHS does recommend that a static device validation according to posture be conducted if the device is to be used in a setting in which patients are not seated quietly in an upright position (O'Brien et al. 1993). This is necessary since readings are very sensitive to the posture of body and arm, body movements, and vibrations during mobility in a vehicle or during walking (Zheng, Giovannini, and Murray, 2012; Koo et al. 2007). We found this to be the case from the results of the pre-eclampsia trial.

Because of the immediate and dire health risks of pre-eclampsia, pregnant women in low-resource hospitals require precise and regular blood pressure measurement. The WHO has blood pressure monitors on its list of core medical equipment and recommends clinicians frequently monitor blood pressure of patients at risk for pre-eclampsia and eclampsia (WHO, 2008; WHO, 2011). In high resource settings, automatic blood pressure monitoring systems are used to monitor blood pressure levels in pre-eclamptic patients at timed intervals since patients with pre-eclampsia may be required to be monitored as often as every 15 minutes. Based on the physiological characteristics of blood pressure vessels in pregnant women, it is important that these monitors are validated specifically for pregnant women (Amoore, 2006). The price range of automatic monitors validated for pregnant women cost upwards of $1,000, which is prohibitively high for low-income settings. Furthermore, manual blood pressure monitors require constant care from staff; something that may be difficult in settings in which the number of staff and clinicians is limited.

The Microlife 3AS1-2 device was designed in part to meet this need. Commercially available for less than $40, it has been validated according to BHS guidelines in a study of 45 pregnant and pre-eclamptic women,

achieving an overall grade of B/A (Nathan, 2015). When tested under BHS guidelines in pregnant patients, both our test device and the Microlife 3AS1-2 achieved a grade A/A. For the systolic pressures, the mean difference between the auscultatory standard and the Microlife 3AS1-2 was -2.9 ± 7.4 mmHg, compared to 1.1 ± 9.2 mmHg for our test device. For diastolic pressure, the mean difference between the auscultatory standard and the Microlife 3AS1-2 was 0.3 ± 5.0 mmHg, compared to 0.7 ± 8.7 mmHg for our device. ISO standards require a standard deviation < 8 mmHg; our test device nearly met this standard. To date, there are no reports evaluating the Microlife 3AS1-2 under real clinical conditions which include patient movement and various postures. Moreover, because the cuff requires manual inflation, it cannot be used for automatic monitoring at regular intervals. This is of particular importance in short-staffed wards in low-resource settings.

In light of the needs of low-resource hospitals, the oscillatory, automated BP sphygmomanometer we describe has the potential to provide a low-cost and durable option for central and district hospitals while also maintaining the high accuracy level seen in commercial-grade systems in a controlled environment. While promising, results of this study indicate that the test device will require future algorithm improvements to reduce sensitivity to subject motion and changes in subject posture since the majority of subjects in the pre-eclampsia trial were lying down when measurements were taken. Upon improvements, a static device validation according to posture, a larger subject population, especially in low-resource settings, and a wider range of blood pressures as referenced in BHS guidelines are required along with a clinical validation according to international standards (ANSI/AAMI/ISO, 2013). Additionally, development of the device to be robust and to identify to the user when it needs maintenance or repair, and addition of memory storage will be necessary. Once validated, the device could enable nurses and clinicians to provide accurate diagnoses and tracking of blood pressure and to provide more effective care to at-risk women.

Conclusions

For maternal healthcare providers in resource-limited settings, there is a pressing need for an appropriate blood pressure monitor that is optimized for pre-eclamptic and eclamptic women. The low-cost, automatic sphygmomanometer device described here differed by less than 15 mmHg for over 90% of subjects when validated in a controlled environment in pregnant and healthy volunteer populations, respectively. When evaluated against the Dinamap Procare 400 in women at risk for pre-eclampsia in a low-resource maternity ward, the test device differed by an average of 2.9 mmHg and -5.4 mmHg for systolic and diastolic pressures, respectively, while the Dinamap differed from the gold standard auscultatory method by 0 mmHg and -3.7 mmHg for systolic and diastolic pressures, respectively. The test device accuracy was lower when patients were moving or not seated during measurement; therefore, while the device has the potential to provide low-resource hospitals with an affordable, accurate option for regular BP monitoring, algorithm improvements are needed to reduce sensitivity to subject motion and posture in order to enable clinicians to track BP in at-risk women in a typical low-resource maternity ward.

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Author contributions

PB, RM, ZMO, and RRK conceptualized the study; LC, TY, and KM developed the novel test device; LC, SM, ECK, HN, HMF, TY, and KM collected data; LC, ES, TY, KM, ZMO, and RRK contributed to data analysis; LC and ES wrote the manuscript. All authors contributed to editing and approval of the manuscript.

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