Development Engineering 2 (2017) 99–106

Contents lists available at ScienceDirect

Development Engineering

journal homepage: www.elsevier.com/locate/deveng

Cost effectiveness of medical devices to diagnose pre-eclampsia in low-resource settings

Zoë M. McLaren[a,*], Alana Sharp[a], John P. Hessburg[b], Amir Sabet Sarvestani[c], Ethan Parker[a], James Akazili[d], Timothy R.B. Johnson[e], Kathleen H. Sienko[b,e,f]

[a] Health Management and Policy, School of Public Health, University of Michigan, 1415 Washington Heights, Ann Arbor, MI 48109-2029, USA
[b] Department of Biomedical Engineering, College of Engineering, University of Michigan, USA
[c] Design Science Program, University of Michigan, USA
[d] Navrongo Health Research Centre, Navrongo, Upper East, Ghana
[e] Department of Obstetrics & Gynecology, Medical School, University of Michigan, USA
[f] Department of Mechanical Engineering, College of Engineering, University of Michigan, USA

ARTICLE INFO

MSC code:
90B99

Keywords:
Cost-effectiveness analysis
Medical devices
Maternal mortality
Pre-eclampsia
Low-income and middle-income countries
Global health
Low-resource settings

ABSTRACT

Background: Maternal mortality remains a major health challenge facing developing countries, with pre-eclampsia accounting for up to 17% of maternal deaths. Diagnosis requires skilled health providers and devices that are appropriate for low-resource settings. This study presents the first cost-effectiveness analysis of multiple medical devices used to diagnose pre-eclampsia in low- and middle-income countries (LMICs).

Methods: Blood pressure and proteinuria measurement devices, identified from compendia for LMICs, were included. We developed a decision tree framework to assess the cost-effectiveness of each device using parameter values that reflect the general standard of care based on a survey of relevant literature and expert opinion. We examined the sensitivity of our results using one-way and second-order probabilistic multivariate analyses.

Results: Because the disability-adjusted life years (DALYs) averted for each device were very similar, the results were influenced by the per-use cost ranking. The most cost-effective device combination was a semi-automatic blood pressure measurement device and visually read urine strip test with the lowest combined per-use cost of $0.2004 and an incremental cost effectiveness ratio of $93.6 per DALY gained relative to a baseline with no access to diagnostic devices. When access to treatment is limited, it is more cost-effective to improve access to treatment than to increase testing rates or diagnostic device sensitivity.

Conclusions: Our findings were not sensitive to changes in device sensitivity, however they were sensitive to changes in the testing rate and treatment rate. Furthermore, our results suggest that simple devices are more cost-effective than complex devices. The results underscore the desirability of two design features for LMICs: ease of use and accuracy without calibration. Our findings have important implications for policy makers, health economists, health care providers and engineers.

1. Introduction

Maternal mortality remains a major health challenge facing developing countries. Each year more than 280,000 women die due to complications related to childbirth, with the vast majority of these deaths occurring in low-income countries (Lozano et al., 2011). Very few countries achieved the Millennium Development Goal 5 of reducing maternal mortality by three-quarters by 2015 (Victora et al., 2015). In low-income countries pre-eclampsia accounts for 11–17% of maternal mortality (Say et al., 2014). Pre-eclampsia is characterized by high blood pressure and elevated levels of protein in the urine. A diagnosis of pre-eclampsia is made if blood pressure is above 140/90 mmHg and there is more than 30 mg/dL of protein in the urine after 20 weeks of gestation (Sibai et al., 2005). When not properly managed, pre-eclampsia may progress to eclampsia, which is characterized by the onset of seizures and can lead to dangerous complications such as stroke, heart failure, thrombosis, systemic endothelial dysfunction, HELLP syndrome, placental abruption, or even death (Sibai et al., 2005). The majority of deaths due to pre-eclampsia are preventable if the symptoms can be identified and if treatment can be

* Corresponding author.
E-mail address: zmclaren@umich.edu (Z.M. McLaren).

http://dx.doi.org/10.1016/j.deveng.2017.06.002
Received 31 December 2015; Received in revised form 29 June 2017; Accepted 29 June 2017
Available online 03 July 2017

administered in a timely manner. Treatment for pre-eclampsia consists of medical and surgical options, including the administration of magnesium sulfate and delivery through induction of labor or cesarean section (Altman et al., 2002).

The diagnosis of pre-eclampsia requires not only skilled health providers, but accurate medical devices that are appropriate for target settings, enabling users to identify pre-eclamptic women when the condition can be managed. In low- and middle-income countries (LMICs) access to the types of medical devices used to diagnose pre-eclampsia in high-income countries is hindered by high cost, limited trained users and inadequate distribution channels. A recent Lancet Commission called for collective approaches by academia, private sectors, non-governmental and international organizations, and ministries of health to prioritize pressing needs, co-identify appropriate solutions, and devise sustainable implementation plans (Howitt et al., 2012). Cost-effectiveness analysis provides a unifying framework to guide the allocation of scarce resources to reduce maternal mortality and morbidity. It has important implications for health policy, health care provision, and clinical and biomedical engineering.

Few studies have examined the cost-effectiveness of devices or procedures to reduce maternal mortality in LMICs. Tsu et al. examined the cost-effectiveness of the active management of third-stage labor (Tsu et al., 2009). Shmueli et al. performed an economic assessment of screening for pre-eclampsia using uterine artery Doppler and serum biomarkers relative to no screening in an Israeli healthcare system (Shmueli et al., 2012). Simon et al. assessed the cost-effectiveness of using magnesium sulfate for pre-eclampsia in low- and high- income countries, and the incremental cost of preventing one case of eclampsia (Simon et al., 2006). Hadker et al. found a novel diagnostic test to be more cost effective in managing a typical pregnancy than blood tests, urine tests, and uterine artery Doppler ultrasounds from the perspective of the UK health system (Hadker et al., 2010). Meads et al. compared 27 screening tests in a UK setting and found a no-test, treat-all strategy to be the most cost effective (Meads et al., 2008). The current study is the first to generate and compare cost-effectiveness ratios for multiple medical screening devices specifically designed for use in LMICs.

The purpose of this study is three-fold: (1) to tabulate cost and effectiveness data for medical devices appropriate for diagnosing pre-eclampsia in LMICs, (2) to develop a decision-tree framework for evaluating interventions that improve diagnosis and treatment of pre-eclampsia based on the costs and benefits to society as a whole, and (3) to generate cost-effectiveness estimates to guide decision-making in clinical practice and health policy to ultimately reduce maternal mortality. This study presents findings from a decision analysis model of medical devices used to diagnose pre-eclampsia in the population of pregnant women residing in LMICs from a societal perspective.

2. Methods

To identify the set of medical devices to include in this study we conducted several literature searches using PubMed, SciVerse Scopus, WHO Compendia of New and Emerging Health Technologies, Appropedia's Medical Devices Compendium and Medline. We contacted both health care professionals in the field of maternal health and product developers involved in the design and testing of maternal health related medical devices designed for use in LMICs to inquire about prototypes in the pipeline. Of the initial list of 15 devices identified, only eight devices had sufficient cost and effectiveness data to be included in the study (Table 1).

Pre-eclampsia is diagnosed by blood pressure measurement with subsequent confirmation of proteinuria by urinalysis. The mercury sphygmomanometer is the widely accepted “gold standard” manual blood pressure measurement device. The other blood pressure measurement devices in the study are either automatic or semi-automatic and designed for use in LMICs. Both auscultatory and oscillometric

Table 1
Proteinuria and blood-pressure devices.

Device category	Device type	Device name	Description	Per-use cost ($)	Device sensitivity	Device specificity
Diagnostic: Proteinuria	Dipstick Test	CLINITEK Status Microalbumin Strip Test (Guy et al., 2009)	Clinitek Status automated analyzer with single use plastic strips that detect albumin and creatinine in urine.	5.70–5.85	0.955	0.533
		Multistix Pro 10LS (Wilde et al., 2008)	Single use plastic strips that detect proteinuria (visually read).	3.29	0.263	0.729
		Uristik (Viswanathan et al., 2005)	Single use plastic strips that detect glucose and protein in urine (visually read).	0.2	0.680	0.680
		DCA 2000 + (Guy et al., 2009)	Automated, battery-powered device that displays the proteinuria content of a urine sample on an LCD screen.	12.90	0.994	0.840
Diagnostic: Blood-pressure	Auscultatory	Mercury Sphygmo-manometer (Hunyor et al., 1978)	Manual device that uses a mercury column to display the pressure of a cuff inflated around the upper arm. Requires a trained operator to listen to Korotkoff sounds with a stethoscope.	0.009–0.039	0.966	0.877
	Hybrid	Nissei DM-3000 (Duhig et al., 2009)	Hybrid device with manual auscultatory and automatic oscillometric settings, with digital display. This study uses values from the auscultatory setting only.	0.076–0.11	0.918	0.914
	Oscillometric	Spot Vital Signs (Alpert, 2007)	Rechargeable battery-powered device that automatically inflates cuff, obtains blood pressure through a built-in algorithm, and displays result on a digital display.	0.15–0.29	0.931	0.858
		Microlife (de Greeff et al. 2008)	Manually inflated device that automatically determines blood pressure with a built-in algorithm, and displays result digitally.	0.004	0.910	0.905

Notes: Costs are in US 2015 dollars.

blood pressure measurement devices constrict blood flow with an inflatable arm cuff. Oscillometric devices use volumetric changes in the cuff to calculate blood pressure, while auscultatory devices require a stethoscope to listen to Kortokoff sounds in the downstream artery to determine pressure. Single-use dipsticks are the standard proteinuria testing method in LMICs. Multistix Pro 1LS and Bayer Diagnostics India's Uristik include a color chart to determine the amount of protein in the urine. The Siemens Clinitek 50 device with microalbumin strip test and Siemens/Bayer DCA 2000+ Analyzer accept a urine sample and display the protein content numerically.

The appropriate sensitivity and specificity measurements for each device were drawn from the literature (Table 1). We calculated sensitivity values for the blood pressure devices using the bias-corrected modeling methodology of Wan et al., which predicts sensitivity rates based on information on the mean and standard deviation using predictions from regression modeling of studies included in the systematic review parameters (Wan et al., 2010). Costs were obtained from the literature where available, and otherwise directly from the manufacturer or distributor.

We developed a decision-tree framework for a study population of pregnant women in LMICs (Fig. A1). The decision tree models the probability that a pregnant woman is tested, stepwise, first for pre-eclampsia (i.e. blood pressure measurement), followed by confirmatory proteinuria analysis for women with blood pressures above 140/90 mmHg, correctly diagnosed, and treated successfully. Each terminal node reveals the disability-adjusted life years (DALYs) associated with a particular sequence of patient outcomes. We used standard cost-effectiveness methodology to assess costs, DALYs gained relative to the baseline and incremental cost per DALY gained (Gold et al., 1996; Drummond et al., 2005). We identified undominated, absolute dominated and extended dominated interventions. The parameter values in the model reflect the generally available standard of access and care based on our review of the literature and expert opinion (Table 2). We also performed a comprehensive set of sensitivity analyses to evaluate the robustness of our findings to changes in parameter values.

No official measures are recorded for pre-eclampsia testing rates in LMICs, so we assumed that women are tested for pre-eclampsia if they have attended at least four antenatal care visits (51% of pregnancies). This assumption is conservative; many women will be tested for pre-eclampsia during one of the first three pre-natal visits, especially if these visits occur late in the pregnancy. Our estimate of the survival rate of untreated pre-eclampsia comes from a population-based survey of a cohort of over 20,000 pregnant women in six West African countries (Prual et al., 2000). Nevertheless, the sensitivity analysis includes results from the range of parameter values found in the literature (78.8–85.6%) (Prual et al., 2000; Mwinyoglee et al., 1996). We modeled magnesium sulfate injection as the standard management technique for pre-eclampsia because it has been accepted as the “drug of choice” for treating pre-eclampsia and is included on the WHO's list of priority medicines for mothers and children, the package of commodities needed to achieve the Millennium Development Goal 5 (Sheth and Chalmers, 2002). Magnesium sulfate is easy to administer, even in LMICs, and demonstrably extremely effective, with a success rate of 99.2% in a large international trial (Altman et al., 2002). False positives receiving magnesium sulfate should not experience a negative impact on mortality or morbidity. Side effects of the treatment are minimal and rare. The availability of magnesium sulfate is poor in LMICs despite its recent addition to essential drug lists. With little data available about the availability of magnesium sulfate, we used 16% as our best base case estimate based on author's (Johnson) experience, but also examined a wide range of possible values so that our results are generalizable to many settings. If magnesium sulfate is unavailable, clinicians may provide valium or a lytic cocktail, however these alternatives will have little to no effect on mortality rates. Cost of treatment with magnesium sulfate was estimated as $13 and $18 per treatment in low- and middle-income countries, respectively (Simon et al., 2006). The cost of severe morbidity due to eclampsia is $80 and $722 in low- and middle-income countries, respectively (Simon et al., 2006). To calculate DALYs associated with the 3.8% of cases resulting in permanent disability due to severe complications of pre-eclampsia, we used a health-related quality of life (HRQL) weight of 0.25 (Lee et al., 2010; Åberg et al., 2011; World Health Organization, 2004). The only parameters in the model that vary by device are sensitivity and specificity. The time period of analysis capture outcomes for the entire lifespan of the pregnant women in our simulation.

All costs are expressed in 2015 U.S. dollars and, in the absence of available data on training or maintenance costs, reflect only the incremental cost of purchasing the device. The devices are designed to be easy to use and require minimal training; their use can be incorporated into existing provider care and no additional equipment is needed. We therefore do not include provider training, time, or additional equipment costs.

To identify the impact of uncertainty about parameter values on our results we performed one-way sensitivity analyses as well as second-order probabilistic multivariate sensitivity analyses. We performed a standard set of 5000 independent Monte Carlo simulations where the outcome at each node of the decision tree was determined by draws from independent binomial distributions. For parameters that the one-way sensitivity analyses identified as being particularly influential, we examined a wide range of plausible values in the Monte Carlo analysis. Because survival rates with and without access to pre-eclampsia treatment are correlated, we examined two additional scenarios: a high-resource/high-skill environment with higher than base-case survival rates at all terminal nodes and a low-resource/low-skill environment with relatively lower survival rates at all terminal nodes. Analyses were performed with TreeAge Pro 2015.

3. Results

Table 3 shows the main results on the cost-effectiveness of each intervention. Because the DALYs averted for each device were very similar, the results primarily depended on the per-use cost ranking.

Table 2
Parameters, values, and sources used in pre-eclampsia decision tree analysis.

Parameter description	Value	Source
% of pregnancies that are pre-eclamptic	2.80%	WHO Global Survey on Maternal and Perinatal Health 2009 (Sarno, 2004)
% of pregnancies tested for pre-eclampsia	51.00%	WHO Global Health Observatory (World Health Organization, 2011)
Survival rate for undiagnosed or untreated pre-eclampsia	94.40%	(Prual et al., 2000)
% of diagnosed pre-eclampsia treated	16.00%	Varies worldwide; Dr. Johnson
Success rate of treatment among pre-eclamptic pregnancies	99.20%	The Magpie Trial Collaborative Group (Altman et al., 2002)
Survival rate for successfully treated pre-eclamptic pregnancies	99.43%	(World Health Organiztion, 2011; Dr. Martin)
Survival rate for unsuccessfully treated pre-eclamptic pregnancies	94.40%	(Prual et al., 2000; Dr. Martin)
Rate of severe complications for pre-eclampsia survivors	3.80%	(Sibai et al., 2005, Steegers et al., 2010)
HRQL for lifetime following severe complications	0.25	(Lee et al., 2010; Åberg et al., 2011; World Health Organization, 2004)
Life expectancy	55 yrs	
Discount rate	3%	

Table 3
Costs, DALYs averted and incremental cost effectiveness ratios (ICER) for devices used to detect pre-eclampsia.

Device	Total cost of intervention	Incremental cost	DALYs	Incremental effectiveness (DALYs averted)	ICER (cost per DALY gained)
Baseline (no screening)	**0.080**		**0.05137**		
Microlife, Uristik	**0.305**	**0.2243**	**0.04898**	**0.00240**	**94**
Nissei (low), Uristik	***0.322***	***0.0174***	***0.04896***	***0.00002***	***829***
Nissei (high), Uristik	0.339	0.0173	0.04896	0.00000	*
Sphygmo (low), Uristik	***0.369***	***0.0467***	***0.04883***	***0.00013***	***368***
Sphygmo (high), Uristik	0.384	0.0153	0.04883	0.00000	*
Microlife, Multistix	0.452	0.0828	0.05045	−0.00162	*
Sphygmo (low), Multistix	0.457	0.0883	0.05039	−0.00156	*
Nissei (low), Multistix	0.458	0.0895	0.05044	−0.00161	*
Nissei (high), Multistix	0.476	0.1068	0.05044	−0.00161	*
Spot Vital Signs (low), Uristik	0.481	0.1123	0.04892	−0.00009	*
Spot Vital Signs (high), Uristik	0.553	0.1837	0.04892	−0.00009	*
Sphygmo (high), Multistix	0.567	0.1981	0.05039	−0.00156	*
Spot Vital Signs (low), Multistix	0.686	0.3171	0.05042	−0.00160	*
Nissei (low), CLINITEK (low)	**0.716**	**0.3472**	**0.04798**	**0.00085**	**408**
Nissei (low), CLINITEK (high)	0.724	0.0084	0.04798	0.00000	*
Microlife, CLINITEK (low)	0.731	0.0150	0.04801	−0.00003	*
Nissei (high), CLINITEK (low)	0.733	0.0173	0.04798	0.00000	*
Nissei (high), CLINITEK (high)	0.742	0.0257	0.04798	0.00000	*
Spot Vital Signs (high), Multistix	0.757	0.0413	0.05042	−0.00245	*
Microlife, CLINITEK	0.758	0.0418	0.04801	−0.00003	*
Sphygmo (low), CLINITEK (low)	**0.903**	**0.1867**	**0.04780**	**0.00018**	**1055**
Sphygmo (low), CLINITEK (high)	0.914	0.0112	0.04780	0.00000	*
Sphygmo (high), CLINITEK (low)	0.918	0.0153	0.04780	0.00000	*
Sphygmo (high), CLINITEK (high)	0.929	0.0265	0.04780	0.00000	*
Nissei (low), DCA 2000+	0.948	0.0453	0.04784	−0.00004	*
Nissei (high), DCA 2000+	0.965	0.0627	0.04784	−0.00004	*
Microlife, DCA 2000+	0.976	0.0738	0.04787	−0.00007	*
Spot Vital Signs (low), CLINITEK (low)	1.082	0.1792	0.04793	−0.00013	*
Spot Vital Signs (low), CLINITEK (high)	1.094	0.1917	0.04793	−0.00013	*
Spot Vital Signs (high), CLINITEK (low)	1.153	0.2506	0.04793	−0.00013	*
Spot Vital Signs (high), CLINITEK (high)	1.166	0.2631	0.04793	−0.00013	*
Sphygmo (low), DCA 2000+	**1.199**	**0.2959**	**0.04765**	**0.00015**	**2026**
Sphygmo (high), DCA 2000+	1.214	0.0153	0.04765	0.00000	*
Spot Vital Signs (low), DCA 2000+	1.404	0.2057	0.04779	−0.00013	*
Spot Vital Signs (high), DCA 2000+	1.476	0.2771	0.04779	−0.00013	*

Notes: Costs in US 2015 dollars. ICERs from decision tree simulation for testing rates below 100%. Devices ordered by cost of intervention. Effectiveness calculated relative to scenario with no pre-eclampsia. Baseline scenario has no access to diagnostic testing or clinical management (see text). Asterisk (*) indicates that ICER is not applicable due to dominance by prior strategy. These rows are skipped in calculating incremental costs and effectiveness in subsequent rows. Italics indicates extended dominance; see text.

With the lowest combined per-use cost of 0.204 cents and incremental cost-effectiveness ratio of $93.6 per DALY gained relative to a baseline scenario with no access to testing or treatment, the Microlife semi-automatic blood pressure monitor with the Uristik single-use proteinuria strips was the most cost-effective combination of medical devices to improve the diagnosis of pre-eclampsia. The device combinations on the cost-effectiveness frontier (undominated) were, in order of increasing incremental cost-effectiveness ratio: Nissei DM3000/CLINITEK strip test, the sphygmomanometer/CLINITEK strip test, and the sphygmomanometer/DCA 2000+. The SpotVital blood pressure device and the Multistix proteinuria test were strongly dominated in all combinations. To be on the cost-effectiveness frontier, the SpotVital device would need to have a per-use cost that implies well over 10,000 uses at the quoted price, which is implausible in LMICs. Extended (weak) dominance ruled out two combinations: Nissei DM3000/Uristik and sphygmomanometer/Uristik.

We performed one-way sensitivity analyses of the results to changes in our benchmark model parameters (see tornado diagram in Fig. 1). Our results were most sensitive to the specificity rate for the blood pressure device. Our results were insensitive to parameter values that were very high (treatment success rate, survival rate for untreated pre-eclampsia) or very low (rate of pre-eclampsia, rate of severe morbidity due to untreated or unsuccessfully treated pre-eclampsia).

To address the issue that minimal clinical trial data exists to identify some of our benchmark decision tree parameters, we present the results of a comprehensive sensitivity analysis (Table 4). The first column shows results from a set of simulations based on the base case parameters for the most cost-effective device combination of the Microlife blood pressure measurement device with the Uristik proteinuria strips. The largest improvements in the incremental cost-effectiveness ratio (ICER) come from increases in the specificity of the blood pressure measurement (Microlife) and the treatment access rate for pre-eclampsia. It is worth noting that in countries with a life expectancy greater than 65 years, this intervention pays for itself. In no case does the ICER estimate for the Microlife, the most cost-effective pre-eclampsia diagnosis device, exceed the threshold to be considered cost-effective in low-income countries (World Health Organization, 2013).

Survival rates for untreated pre-eclampsia and successfully treated pre-eclampsia are likely to be positively correlated based on overall health status, access to health care, available health resources and the skill level of health care providers. Columns 2 and 3 of Table 4 show the results from a similar sensitivity analysis as Column 1, but using the high-resource and low-resource scenario values. These scenarios typify comparisons of countries (e.g. South Africa vs. Nigeria or India), regions (e.g. urban vs. rural), or facility types (e.g. tertiary hospital

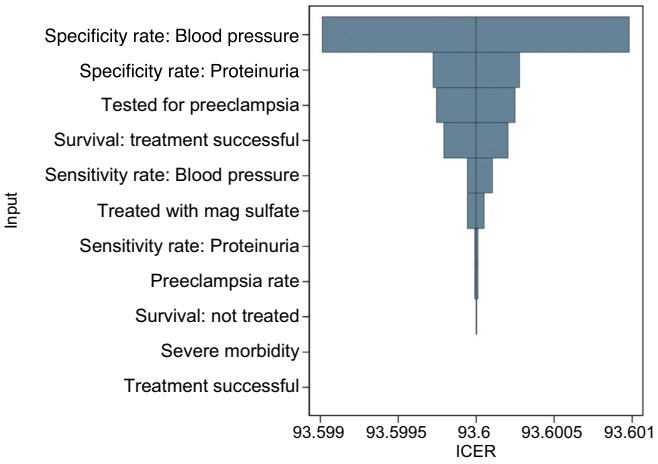

Fig. 1. Tornado diagram: One-way sensitivity analysis of cost-effectiveness of pre-eclampsia intervention to variations in decision tree parameters. *Notes*: Base case = ICER of $93.6/ DALY gained using Microlife/Uristik device combination. Standard tornado diagram calculated from base case parameter values, varying one parameter at a time by 0.1% point. Inputs ranked by size of effect on output mean.

vs. local clinic). The Microlife device had an ICER of $78.88 in the low resource environment relative to the benchmark scenario with no access to testing and $115.05 in the high resource environment.

4. Discussion

Our findings show that among the devices analyzed, the most cost-effective devices for diagnosing pre-eclampsia are simple rather than complex medical devices. For example, the Microlife blood pressure device is manually inflated but provides automated read-outs, and the Uristik strip test is read visually, in comparison with devices such as the SpotVital Signs or the DCA 2000+ which are fully automated. The most cost-effective devices are all low-cost and feasible to implement even in low-income countries. These devices are likely to be at least as cost-effective as screening for pre-eclampsia using uterine artery Doppler and serum biomarkers (Shmueli et al., 2012), prophylactic magnesium sulfate for pre-eclampsia (Simon et al., 2006), community-based distribution of misoprostol for treatment or prevention of postpartum hemorrhage (Sutherland et al., 2010), screening for bacteriuria or syphilis, skilled birth attendance, and management of obstructed labor, post-partum hemorrhage and maternal sepsis (Adam et al., 2005). Furthermore, these devices are well within the range considered cost-effective in low-income countries based on the World Health Organization definition.

Our cost-effectiveness estimates were not particularly sensitive to changes in testing rate, however they were sensitive to changes in device specificity and the treatment access rate (Table 4). Increasing the testing rate by 20% points (from 40% to 60%) had almost no effect on the ICER whereas increasing the blood pressure device specificity by 20% points (from 70% to 90%) reduced the ICER by $180. Intuitively, there is little benefit to identifying pre-eclamptic women when treatment access is low. This has important implications for device design: when treatment rates are low, a reasonably sensitive device that is low in cost is preferred to a highly-sensitive but high-cost device. When it comes to design for global health, the perfect may be the enemy of good.

Our results highlight the importance of two desirable features for LMIC settings: reusability and accuracy in the absence of calibration. High recurring costs, such as single-use components and maintenance costs, limit the cost-effectiveness of these devices in low-income countries. Even though Microlife and Nissei DM3000 require batteries (or AC power) to operate, their batteries are rechargeable rather than disposable. The most cost-effective devices for blood pressure measurement (Microlife, Nissei DM3000 and Mercury sphygmomanometer) are highly accurate and require limited to no calibration.

Other major design features common to the most cost-effective devices are the ability to withstand variable environmental conditions (temperature and humidity), portability and ease of use, which are essential characteristics of devices to be used by health care workers in rural areas. Microlife and Nissei DM3000 have digital screens for displaying blood pressure, which minimizes the likelihood of human error. Uristik and Multistix test strips can be easily interpreted by the immediate change in color in response to the urine droplet.

Our assumptions are all conservative and our results are robust to variance on the dimensions of uncertainty as demonstrated in Table 4. Our estimates understate the DALYs gained from each device in that they don't include the health benefits to the unborn child from improved diagnosis of pre-eclampsia, which are likely quite substantial. These results do not provide accurate absolute cost effectiveness of testing in scenarios where diagnostic equipment are not already accessible and must be purchased; however, the analysis does provide informative data on the relative cost effectiveness of testing women for preeclampsia using these common technologies.

One limitation of our study is the limited data available on several input parameters of our model and on medical device effectiveness and maternal mortality in general. More precise measures of these input parameters will improve our cost-effectiveness estimates to better guide implementation and health policy. Values from standardized trials similar to the MAGPIE trial that compare effectiveness across devices and across settings would be ideal. We have addressed this limitation with a comprehensive set of probabilistic sensitivity analyses, however, additional effectiveness and survival data would enable us to widen the range of devices examined and draw more specific policy implications from the study. We are not able to model the full cost structure due to limited data on labor costs for training and delivering the test, device maintenance costs, time patients spend traveling and waiting for care, costs of follow-on-care following serious complications due to pre-eclampsia and offsetting health care cost savings due to prevented cases of eclampsia.

Cost-effectiveness analysis considers every stage of implementation in the local environment from when the patient presents at a health facility through diagnosis, treatment and patient outcome. By taking into account the big picture, it makes implicit tradeoffs explicit such as diagnosis versus treatment or cost versus effectiveness. In settings where treatment is rationed or unavailable, the most effective diagnostic device is not necessarily the most desirable, but rather the one that achieves a certain threshold of effectiveness at the lowest cost. Our results provide additional evidence that "hand me down" technology from high-income

Table 4
Sensitivity analysis for base case, low-resource and high-resource country scenarios.

	ICER Base case	ICER Low resource	ICER High resource
Tested rate			
20	93.58	78.85	114.95
40	93.63	78.89	115.02
51 (base case)	93.62	78.88	115.05
60	93.62	78.90	115.05
80	93.61	78.89	115.06
Treated rate			
16 (base case)	93.62	78.88	115.05
20	76.10	64.12	93.52
40	41.04	34.60	50.42
60	29.36	24.76	36.06
80	23.52	19.84	28.87
Device sensitivity, Microlife			
70	119.59	100.77	146.99
80	105.49	88.90	129.71
90	94.57	79.71	116.21
91 (base case)	93.62	78.88	115.05
95	89.95	75.81	110.55
99	86.62	72.99	106.47
99.5	86.22	72.67	105.96
Device sensitivity, Uristik			
68 (base case)	93.62	78.88	115.05
70	91.10	76.79	111.99
80	80.47	67.83	98.89
90	72.18	60.84	88.74
95	68.70	57.91	84.43
99	66.17	55.78	81.33
99.5	65.88	55.52	80.94
Device specificity, Microlife			
70	278.55	234.62	342.39
80	188.34	158.65	231.49
90	98.13	82.68	120.60
90.5 (base case)	93.62	78.88	115.05
95	53.03	44.69	65.15
99	16.95	14.30	20.63
99.5	12.44	10.50	15.25
Device specificity, Uristik			
68 (base case)	93.62	78.88	115.05
70	88.51	74.57	108.77
80	62.96	53.05	77.36
90	37.41	31.54	45.95
95	24.63	20.78	30.24
99	14.41	12.17	17.68
99.5	13.14	11.09	16.10
Discount rate			
0%	0.02	0.02	0.02
3% (base case)	93.62	78.88	115.05
6%	−0.03	−0.03	−0.03
Life expectancy			
55 (base case)	93.62	78.88	115.05
65	0.07	0.07	0.07
HRQL			
0.2	167.40	123.91	257.45
0.25 (base case)	93.62	78.88	115.05
0.3	64.98	57.87	74.08

Notes: Table reports simulation results of ICERs from varying the mean of each parameter as indicated for Microlife/Uristik device combination. Each cell represents a separate simulation. Low-resource country scenario (e.g., Nigeria) has high general mortality: untreated survival 92.4%; treated survival 98.93%. High-resource country scenario (e.g., South Africa) has low general mortality: untreated survival 96.4%; treated survival 99.93%.

countries is unlikely to be appropriate in LMICs because developed countries have focused on the most effective solution, regardless of cost (Howitt et al., 2012; Malkin, 2007; Free, 2004).

Our results have important implications for routine healthcare provision in both clinical and policy contexts. While other studies have evaluated the cost effectiveness of screening and treatment strategies in high income countries, to our knowledge no other study has evaluated the cost effectiveness of medical screening technologies designed for use in LMIC. Cost-effectiveness analysis is an important tool that incorporates information about the local environment to produce tailored policies, devices, and procedures. These are the type of results needed to inform evidence-based medicine, which allows policy-makers to standardize procedures in LMICs and thereby reduce maternal mortality. This study was designed to help translate scientific advances into policy and practice in LMICs. We provide a clear framework for decision-making and assess the areas that are most sensitive to uncertainty. In the era of implementation science and implementation engineering, cost-effectiveness should guide not only the development of new devices and procedures but also the implementation and evaluation (Johnson, 2013).

Authors' contributions

Supervised the development of the decision tree framework and generation of the analysis parameters, designed the cost-effectiveness analyses: ZMM. Identified and selected medical devices for inclusion in the study and obtained parameter values for use in the analysis: JPH ASS JA. Contributed to the development of the compendia used in the study: ASS. Performed the cost-effectiveness analyses in TreeAge: ZMM EP AS. Contributed to the development of the decision tree and analysis parameters: TRBJ. Conceived of the study, conceived of and supervised the creation of one of the compendia used in the study, supervised data collection: KHS. Drafted the manuscript: ZMM ASS AS TRBJ KHS. Read and approved the final manuscript: ZMM JPH ASS EP AS JA TRBJ KHS.

Funding

University of Michigan Center for Global Health Jr. Faculty Engagement Award (Sienko); University of Michigan Institute for Research on Women and Gender's Faculty Seed Grant (McLaren); Fogarty International Center at the National Institutes of Health, Grant Number 1R24TW008814-01: Ghana-Michigan Postdoctoral And Research Training NetwoRk (PARTNER) Program (Sienko, Akazili); National Science Foundation Graduate Research Fellowship (Sabet Sarvestani); University of Michigan Third Century Initiative.

Conflicts of interest

None declared.

Role of the funding source

Funding organizations had no role in study design, data analysis, and the writing; the contents are the sole responsibility of the authors. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Ethical approval

Not required.

Acknowledgements

The authors are grateful to David Hutton, James G. Kahn, David Mendez, Lisa Prosser, two anonymous referees and participants at the American Society of Health Economics conference for their suggestions and comments. Yi Mao provided research assistance and Ann Stewart provided technical editing services.

Appendix

Complete decision tree representing the pathways of diagnosis and treatment for a pre-eclamptic pregnant woman presenting at an antenatal care facility in a developing country.

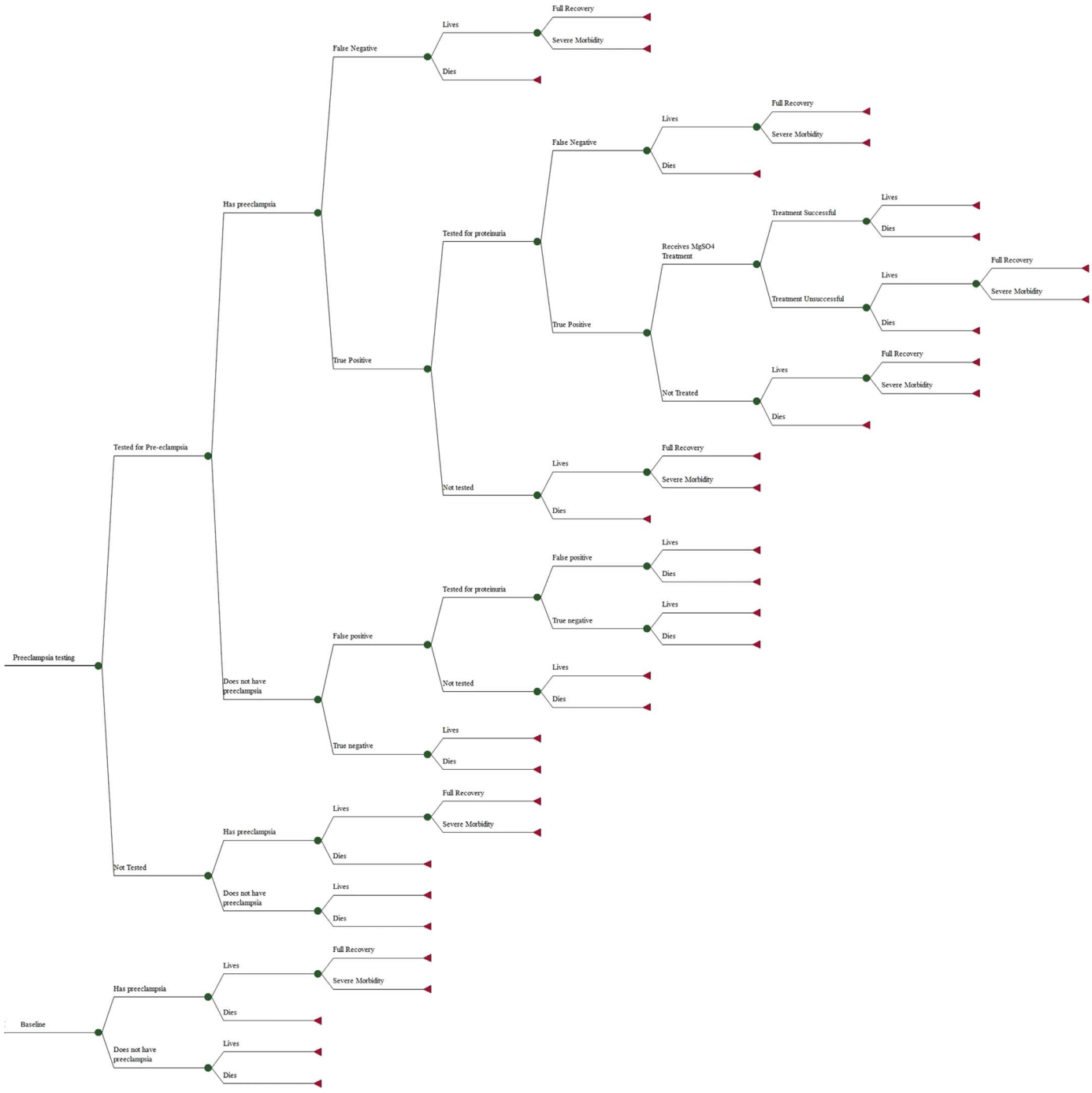

Fig. A1. A standard decision tree representing the pathways of diagnosis and treatment for a pre-eclamptic pregnant woman presenting at an antenatal care facility in a LMIC.

Notes: Full analysis includes analogous branches of decision tree for non-pre-eclamptic pregnant woman. Triangles represent terminal nodes. Parameter values are found in Table 2.

References

Åberg, F., Mäklin, S., Räsänen, P., Roine, R.P., Sintonen, H., Koivusalo, A., et al., 2011. Cost of a quality adjusted life year in liver transplantation: the influence of the indication and the model for end-stage liver disease score. Liver Transplant. 17 (11), 1333–1343.

Adam, T., Lim, S.S., Mehta, S., Bhutta, Z.A., Fogstad, H., Mathai, M., et al., 2005. Achieving the millennium development goals for health: cost effectiveness analysis of strategies for maternal and neonatal health in developing countries. Br. Med. J. 331 (7525), 1107–1110.

Alpert, B.S., 2007. Validation of the Welch Allyn Spot vital signs blood pressure device according to the ANSI/AAMI SP10: 2002. Accuracy and cost-efficiency successfully combined. Blood Press. Monit. 12 (5), 345–347.

Altman, D., Carroli, G., Duley, L., Farrell, B., Moodley, J., Neilson, J., et al., 2002. Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled Trial. Lancet 359 (9321), 1877.

Drummond, M.F., Sculpher, M.J., Torrance, G.W., O'brien, B.J., Stoddart, G.L., 2005. Methods for the Economic Evaluation of Health Care Programmes. Oxford University Press, USA.

Duhig, K.E., De Greeff, A., Van Der Westhuizen, A., Baker, E., Shennan, A.H., 2009. Validation of the Nissei DS-400 in a low-resource setting. Blood Press. Monit. 14 (3), 132.

Free, M.J., 2004. Achieving appropriate design and widespread use of health care technologies in the developing world: overcoming obstacles that impede the adaptation and diffusion of priority technologies for primary health care. Int. J. Gynecol. Obstet. 85, S3–S13.

Gold, M.R., Siegel, J.E., Russell, L.B., Weinstein, M.C., 1996. Cost-Effectiveness in Health and Medicine. Oxford University Press, USA.

de Greeff, A., Nathan, H., Stafford, N., Liu, B., Shennan, A.H., 2008. Development of an accurate oscillometric blood pressure device for low resource settings. Blood Press. Monit. 13 (6), 342–348.

Guy, M., Newall, R., Borzomato, J., Kalra, P.A., Price, C., 2009. Diagnostic accuracy of the urinary albumin: creatinine ratio determined by the CLINITEK Microalbumin and DCA 2000+ for the rule-out of albuminuria in chronic kidney disease. Clin. Chim. Acta 399 (1–2), 54–58.

Hadker, N., Garg, S., Costanzo, C., Miller, J.D., Foster, T., van der Helm, W., et al., 2010. Financial impact of a novel pre-eclampsia diagnostic test versus standard practice: a decision-analytic modeling analysis from a UK healthcare payer perspective. J. Med. Econ. 13 (4), 728–737.

Howitt, P., Darzi, A., Yang, G.Z., Ashrafian, H., Atun, R., Barlow, J., et al., 2012. Technologies for global health. Lancet 380 (9840), 507–535.

Hunyor, S., Flynn, J., Cochineas, C., 1978. Comparison of performance of various sphygmomanometers with intra-arterial blood-pressure readings. Br. Med. J. 2 (6131), 159.

Johnson, T., 2013. Implementing evidence-based science to improve women's health globally. Int. J. Gynaecol. Obstet..

Lee, B.Y., Wateska, A.R., Bailey, R.R., Tai, J.H.Y., Bacon, K.M., Smith, K.J., 2010. Forecasting the economic value of an Enterovirus 71 (EV71) vaccine. Vaccine 28 (49), 7731–7736.

Lozano, R., Wang, H., Foreman, K.J., Rajaratnam, J.K., Naghavi, M., Marcus, J.R., et al., 2011. Progress towards Millennium Development Goals 4 and 5 on maternal and child mortality: an updated systematic analysis. Lancet 378 (9797), 1139–1165.

Malkin, R.A., 2007. Design of health care technologies for the developing world. Annu. Rev. Biomed. Eng. 9, 567–587.

Meads, C.A., Cnossen, J.S., Meher, S., Juarez-Garcia, A., ter Riet, G., Duley, L., et al., 2008. Methods of prediction and prevention of pre-eclampsia: systematic reviews of accuracy and effectiveness literature with economic modelling. Health Technol. Assess. 12 (6), 1–270.

Mwinyoglee, J., Amoko, D., Simelela, N., Marivate, M., 1996. Eclampsia at Ga-Rankuwa Hospital. South Afr. Med. J. Cape Town Med. Assoc. South Afr. 86, 1536–1539.

Prual, A., Bouvier-Colle, M., De Bernis, L., Breart, G., 2000. Severe maternal morbidity from direct obstetric causes in West Africa: incidence and case fatality rates. Bull. World Health Organ. 78 (5), 593–602.

Sarno L., 2004. Maternal Health Tabulations. Guideline development, Research priorities, Evidence synthesis, Applicability of evidence, Transfer of knowledge (G.R. E.A.T. project). World Health Organization Reproductive Health Research Team for Improving Maternal and Perinatal Health.

Say, L., Chou, D., Gemmill, A., Tunçalp, Ö., Moller, A.B., Daniels, J., et al., 2014. Global causes of maternal death: a WHO systematic analysis. Lancet Glob. Health 2 (6), e323–e333.

Sheth, S.S., Chalmers, I., 2002. Magnesium for preventing and treating eclampsia: time for international action. Lancet 359 (9321), 1872.

Shmueli, A., Meiri, H., Gonen, R., 2012. Economic assessment of screening for pre-eclampsia. Prenat. Diagn..

Sibai, B., Dekker, G., Kupferminc, M., 2005. Pre-eclampsia. Lancet 365 (9461), 785–799.

Simon, J., Gray, A., Duley, L., 2006. Cost-effectiveness of prophylactic magnesium sulphate for 9996 women with pre-eclampsia from 33 countries: economic evaluation of the Magpie Trial. BJOG: Int. J. Obstet. Gynaecol. 113 (2), 144–151.

Steegers, E.A., von Dadelszen, P., Duvekot, J.J., Pijnenborg, R., 2010. Pre-eclampsia. Lancet 376 (9741), 631–644.

Sutherland, T., Meyer, C., Bishai, D.M., Geller, S., Miller, S., 2010. Community-based distribution of misoprostol for treatment or prevention of postpartum hemorrhage: cost-effectiveness, mortality, and morbidity reduction analysis. Int. J. Gynecol. Obstet. 108 (3), 289–294.

Tsu, V.D., Levin, C., Tran, M.P.T., Hoang, M.V., Luu, H.T.T., 2009. Cost-effectiveness analysis of active management of third-stage labour in Vietnam. Health Policy Plan. 24 (6), 438–444.

Victora, C.G., Requejo, J.H., Barros, A.J., Berman, P., Bhutta, Z., Boerma, T., et al., 2015. Countdown to 2015: a decade of tracking progress for maternal, newborn, and child survival. Lancet.

Viswanathan, V., Nair, M.B., Suresh, S., Chamukuttan, S., Ambady, R., 2005. An inexpensive method to diagnose incipient diabetic nephropathy in developing countries. Diabetes care 28 (5), 1259–1260.

Wan, Y., Heneghan, C., Stevens, R., McManus, R., Ward, A., Perera, R., et al., 2010. Determining which automatic digital blood pressure device performs adequately: a systematic review. J. Human. Hypertens. 24 (7), 431–438.

Wilde, H.M., Banks, D., Larsen, C.L., Connors, G., Wallace, D., Lyon, M.E., 2008. Evaluation of the Bayer® microalbumin/creatinine urinalysis dipstick. Clin. Chim. Acta 393 (2), 110–113.

World Health Organization, 2004. Global Burden of Disease 2004 Update: Disability Weights for Diseases and Conditions.

World Health Organization, 2011. Global Health Observatory Data Repository. Cambodia. Country Statistics Available on: ⟨http://apps.who.int/ghodata⟩.

World Health Organization, 2013. Choosing Interventions that are Cost Effective (WHO-CHOICE), ⟨http://www.who.int/choice/costs/CER_levels/en/index.html⟩. (Accessed on August 24, 2013).

World Health Organiztion, 2011. World Health Statistics Report.