

# Universal Access to Essential Vital Signs Monitoring

J. Mark Ansermino, MBBCh, FRCPC

Much more than a telephone, today's mobile device has become an integral part of the way we interface with the world. Mobile devices have the computing capability, display, and battery power to become powerful medical devices that measure vital signs and provide intelligent interpretation or immediate transmission of information. The widespread adoption of mobile devices, even in low-resource settings, promises to make vital signs monitoring available anywhere and at low cost. This readily available computing power will also extend the utility of vital signs monitoring to new clinical indications, especially with the use of additional processing and integration of information. This review will focus on the universal promotion of pulse oximetry and advanced processing of plethysmography to assess variables such as respiratory rate, capillary refill time, and fluid responsiveness, and how these measurements may assist with perioperative monitoring, diagnosis, and management of pneumonia in children and preeclampsia in pregnancy when combined with mobile devices. (Anesth Analg 2013;117:883–90)

The high cost and limited availability of health care at high-level hospital settings are increasingly motivating the need to find new models of health care delivery in both the developed and developing worlds. Especially in the latter, there is a particular need for self-monitoring and community diagnosis of medical conditions. The near-ubiquity of mobile phones is a central element in the promise of mobile technologies for health care. With inexpensive mobile phones and the global penetration of phone networks, tens of millions of citizens who previously never had regular access to a fixed-line telephone or a computer now use mobile devices as daily tools for communication and data transfer. There are 6.8 billion mobile phone subscriptions in the world, with 89% penetration in developing countries. (Table 1, Ref. 1). Africa alone had 620 million mobile devices in 2011, with estimates of 735 million by December 2012 (Table 1, Ref. 2). The adoption of mobile technologies to deliver health care will leverage this widespread use of mobile phones and other mobile devices and will offer personal toolkits, including vital sign monitoring, for predictive, participatory, and preventative care in rapidly growing consumer sectors (Table 1, Ref. 3).

This review will focus on the universal promotion of pulse oximetry in anesthesia and on new indications for intelligent applications of pulse oximetry when combined with mobile devices such as smart phones and tablet computers to assist with perioperative monitoring, diagnosis, and management of pneumonia in children and preeclampsia in pregnancy. Since its introduction into the operating room in the 1980s, pulse oximetry has been routinely used to intraoperatively monitor patients who are under anesthesia. The use of pulse oximetry has now spread throughout

the hospital (in the intensive care unit, the emergency department, and on the ward) so that any patient with unstable oxygen levels will be monitored. Determination of arterial oxygen saturation with pulse oximetry is now in such ubiquitous use that it has been called the "fifth vital sign."<sup>1</sup> Beyond anesthesia, efficient and affordable pulse oximetry monitoring systems, for in-facility and at-home use, will support enhanced diagnosis, monitoring and treatment for a wide range of clinical conditions.

## PULSE OXIMETRY IN ANESTHESIA

The introduction and then widespread adoption of technology to monitor patients during anesthesia has undoubtedly been a significant contributor, along with training and safer drugs, to the >10-fold reduction in anesthesia-related mortality.<sup>2</sup> Despite the current lack of clinically demonstrated improvement in outcomes, effectiveness, and efficiency, with the use of monitoring technology,<sup>3</sup> few clinicians would wish to forego the use of these monitoring devices. In addition, monitors such as pulse oximeters have become widely accepted as essential during anesthesia and are even mandatory in the United Kingdom, Canada, the United States, Australia, New Zealand, much of Europe and South America, and many other countries around the world. Anesthesia today is very safe in most developed countries, with mortality rates attributable to anesthetic complications at 34 per million.<sup>4</sup> However, there are still places where the mortality rate is 1000 times higher than this.<sup>5</sup> Many of these deaths are related to hypoxia, presumably due to a lack of training and resources.

There are still many locations globally where pulse oximeters are not routinely used during anesthesia, as they are not available.<sup>6</sup> An estimated 77,000 operating rooms are without oximeters<sup>6</sup> and many other locations that would benefit from technology to improve safety, such as recovery rooms, intensive care units, and emergency rooms. A significant challenge to the widespread adoption of life-saving monitoring technologies has been the cost associated with purchase, use, and maintenance of the monitoring devices.

Many efforts are underway to address this gap in access to technology. As a commitment to this cause, the Quality and Safety of Practice Committee of the World Federation of Societies of Anesthesiologists identified the need for provision of pulse oximeters for use on every patient

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Accepted for publication June 17, 2013.

Funding: Not funded.

Conflict of Interest: See Disclosures at the end of the article.

Reprints will not be available from the author.

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DOI: 10.1213/ANE.0b013e3182a1f22f

**Table 1. Web Sites Referenced Within the Text**

Reference no.	Web site
1	International Telecom Union. The world in 2013. ICT Facts and Figures. Available at: <a href="http://www.itu.int/en/ITU-D/Statistics/Documents/facts/ICTFactsFigures2013.pdf">http://www.itu.int/en/ITU-D/Statistics/Documents/facts/ICTFactsFigures2013.pdf</a> . Accessed July 26, 2013.
2	Global Systems for Mobile Communications Association (GSMA). African mobile observatory: driving economic and social development through mobile services. Available at: <a href="http://www.gsma.com/publicpolicy/wp-content/uploads/2012/04/africamoewebfinal.pdf">http://www.gsma.com/publicpolicy/wp-content/uploads/2012/04/africamoewebfinal.pdf</a> . Accessed April 8, 2013.
3	Global Systems for Mobile Communications Association (GSMA). Touching lives through mobile health assessment of the global market opportunity. Available at: <a href="http://www.gsma.com/connectedliving/wp-content/uploads/2012/03/gsmawctouchinglivessthroughmobilehealthreport.pdf">http://www.gsma.com/connectedliving/wp-content/uploads/2012/03/gsmawctouchinglivessthroughmobilehealthreport.pdf</a> . Accessed June 6, 2013.
4	World Health Organization. Patient Safety Pulse Oximetry Project 2012. Available at: <a href="http://who.int/patientsafety/safesurgery/pulse_oximetry/en/index.html">http://who.int/patientsafety/safesurgery/pulse_oximetry/en/index.html</a> . Accessed July 5, 2012.
5	World Health Organization. Safe Surgery Saves Lives 2009. Available at: <a href="http://www.who.int/patientsafety/safesurgery/en/index.html">http://www.who.int/patientsafety/safesurgery/en/index.html</a> . Accessed July 5, 2012.
6	Lifebox Annual Review 2012. Saving lives through safer surgery. Available at: <a href="http://www.lifebox.org/2012-annual-review/">http://www.lifebox.org/2012-annual-review/</a> . Accessed April 8, 2013.
7	Mobi Health News. Masimo offers iPhone-enabled pulse ox to climbers, pilots. Available at: <a href="http://mobihealthnews.com/19563/masimo-offers-iphone-enabled-pulse-ox-to-climbers-pilots/">http://mobihealthnews.com/19563/masimo-offers-iphone-enabled-pulse-ox-to-climbers-pilots/</a> . Accessed May 30, 2013.
8	Saving Lives at Birth: A Grand Challenge for Development. PIERS on the move: Preeclampsia Integrated Estimate of RiSk assessment on a mobile phone. Available at: <a href="http://savinglivesatbirth.net/summaries/37">http://savinglivesatbirth.net/summaries/37</a> . Accessed December 14, 2012.
9	WaveFront Technology. WaveFront Flow Meter. Available at: <a href="http://www.thormed.com/index.php?page=products&amp;id=spiro4">http://www.thormed.com/index.php?page=products&amp;id=spiro4</a> . Accessed December 14, 2012.

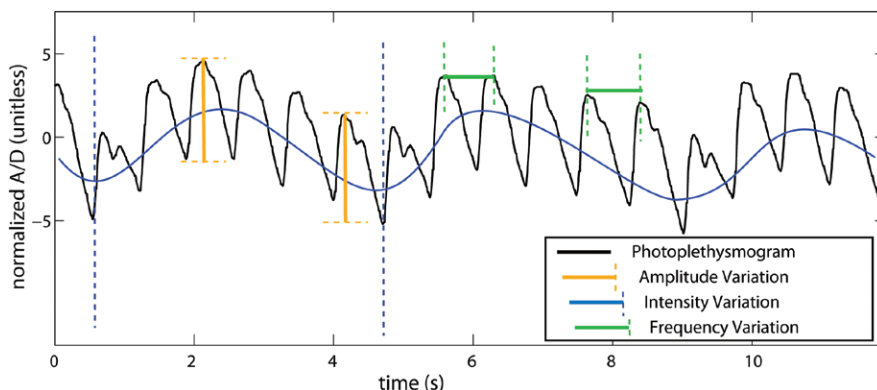
undergoing anesthesia as a priority for improving patient safety.<sup>7</sup> The World Health Organization (WHO) is also aiming to improve safety in surgery and anesthesia on a global scale through the Global Oximetry initiative (Table 1, Ref. 4) and Safe Surgery Saves Lives (Table 1, Ref. 5). Along these lines, representatives of the Association of Anesthetists of Great Britain and Ireland, the World Federation of Societies of Anesthesiologists, and the Harvard School of Public Health created a charity called the “Lifebox” to facilitate access to pulse oximeters suitable for use in operating rooms around the world, along with training and support for the introduction of the WHO checklist for surgery.<sup>8</sup> The Lifebox oximeter is powered by battery or electrical mains power, has configurable alarms, a waveform, and changes tone as the saturation decreases. The device and training materials are supplied for \$250 (£160; €196), largely supported by international donations. This innovative program is rapidly gaining momentum and has currently (2012) donated 4000 pulse oximeters to >70 countries with support from a wide range of individuals, national societies, journals, and non-governmental organizations (Table 1, Ref. 6).

The utility of pulse oximetry could be significantly advanced if it was more mobile and if additional features of the photoplethysmographic signal produced by a pulse oximeter could be reliably extracted.

**ADVANCED PROCESSING OF THE PHOTOPLETHYSMOGRAPH**

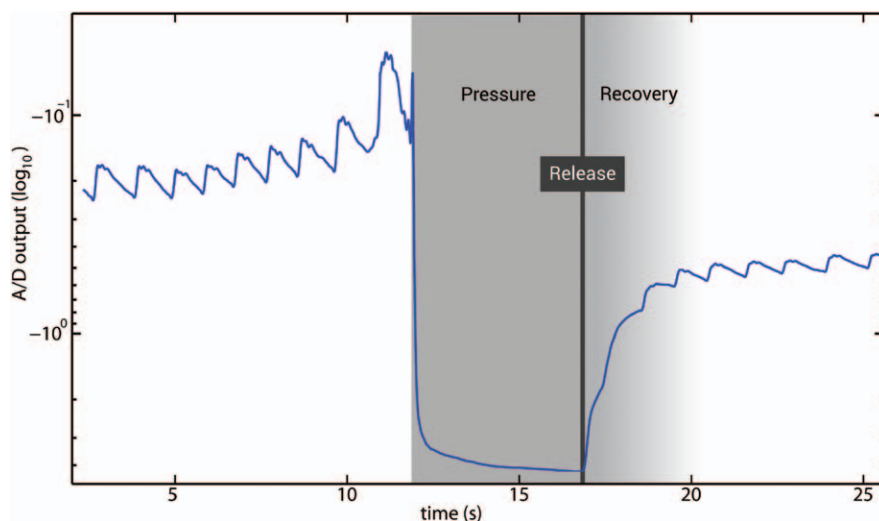
Pulse oximeters typically produce a graphical display of the change in blood volume called the photoplethysmograph (PPG). The PPG is currently used to identify the quality of the signal (artifact identification) and to estimate the heart rate. The unrealized potential of providing additional information in the PPG was reviewed by Murray and Foster.<sup>9</sup> The PPG waveform can provide additional physiological measures, including respiratory activity, vasomotor tone, autonomic status, fluid responsiveness, stroke volume, cardiac output, hemoglobin, and even blood glucose.<sup>10,11</sup> PPG measurement on mobile computing devices would significantly extend the usefulness of these measurements.

A number of algorithms have been proposed for respiratory rate (RR) estimation from the PPG.<sup>12,13</sup> These methods rely on one or more effects of respiration (amplitude, frequency, and intensity) on the PPG (Fig. 1).<sup>14</sup> Commercial implementations of RR extraction have recently received regulatory approval in higher-end pulse oximeter devices. Another potential use of the PPG is the semiautomated measurement of capillary refill time (CRT). CRT is defined as the time taken for a distal capillary bed to regain its color (return of blood flow) after pressure has been applied to cause blanching (blood pushed out) (Fig. 2). Manually



**Figure 1.** The effects of respiration on the amplitude, frequency, and intensity of the photoplethysmograph that can be used to estimate the respiratory rate.

**Figure 2.** Photoplethysmograph for the measurement of capillary refill time, demonstrating applied pressure (blood expelled from the finger), release (typical artifact), and recovery of blood flow.



measured CRT has become widely used in adults and children and has been incorporated into advanced life support guidelines as part of the rapid, structured cardiopulmonary assessment of critically ill patients.<sup>15</sup> However, since digitized CRT techniques are unavailable to the practicing clinician, the clinical measurement of CRT is operator dependent and not reproducible. Automated CRT assessment may offer the opportunity to define a new “gold standard” for CRT measurement.<sup>16</sup> Further clinical validation in subjects with prolonged CRT will be required before introduction into clinical practice.

PPG-derived dynamic preload indicators, such as changes in the PPG amplitude ( $\Delta$ POP) and pleth variability index, have been shown to be superior to traditional, invasive, static measures of cardiac preload, such as central venous pressure or pulmonary capillary wedge pressure, when determining fluid responsiveness in adults.<sup>17,18</sup> Dynamic preload indicators are based on the observation that cardiac stroke volume varies with inspiration and expiration. This variation is an indication of fluid responsiveness, with increased variation occurring in patients who responded positively to a fluid bolus. The accuracy of prediction of fluid responsiveness is dependent on many factors such as sinus rhythm, controlled ventilation with large tidal volumes, and on the size and type of fluid bolus.<sup>19</sup>

### **PULSE OXIMETRY FOR DIAGNOSIS AND MANAGEMENT OF PNEUMONIA IN CHILDREN**

Every year, pneumonia kills approximately 2.5 million children younger than 5 years of age, mostly in the low-income countries of Africa and Asia, accounting for more deaths than human immunodeficiency virus-acquired immune deficiency syndrome, malaria and tuberculosis combined.<sup>20</sup> These deaths result from delays in diagnosis, triage, transportation, and treatment. The United Nations' Millennium Development Goal 4 calls for a two-thirds reduction in under-5 mortality by 2015, compared with the 1990 baseline. Progress in mortality reduction, especially due to pneumonia, is still lagging in many underdeveloped and developing countries, where 155 million new episodes of clinical pneumonia occur in children younger than 5 years of age annually.<sup>21</sup> Many of these deaths could be prevented by

early detection and timely administration of simple treatments (e.g., antibiotics, fluids, oxygen). However, almost all of these deaths occur in the developing world, where lack of access to clinical expertise and costly tests often delay diagnosis and treatment and reduce survival. There is an urgent need for a robust, inexpensive device that can guide frontline health care workers to quickly and accurately identify and manage childhood pneumonia, especially in resource-limited environments.

The Global Action Plan for Prevention and Control of Pneumonia, initiated by WHO and United Nations Children's Fund (UNICEF) and an expert panel of clinicians and researchers convened by the WHO,<sup>22</sup> has established that instead of finding new interventions for pneumonia, the integrated global research priority should focus on removing barriers to health care seeking and access for children in developing countries. In particular, research that strengthens community-based case management, a key strategy championed by UNICEF, has emerged as the top priority to reduce childhood mortality due to pneumonia.<sup>23</sup>

The current criteria for diagnosing childhood pneumonia using clinical signs as well as special investigations are plagued with uncertainty, even in the developed world. The diagnostic accuracy of clinical, radiological (chest radiograph), and laboratory tests was found to vary widely.<sup>24</sup> The 4 objective signs that currently constitute the core of the WHO's diagnostic recommendations are fast breathing, chest in-drawing, stridor, and inability to drink.<sup>25</sup> These could be extended to include a low oxygen saturation, as has been suggested in a recent update from the WHO (Fig. 3).<sup>26,27</sup> However, RR is not reliably measured due to the challenging nature of this clinical task.<sup>28</sup> This is even more difficult to measure in smaller children who breathe more rapidly. In addition, increased RR and chest in-drawing were found to be reliable signs of pneumonia only in children younger than 36 months of age.<sup>29</sup> In an emergency department study, RR alone did not discriminate children with and without radiographic pneumonia.<sup>30</sup>

Pulse oximetry is a simple yet conclusive test for hypoxemia that has been shown to correctly identify 20% to 30% more children with hypoxemia than clinical signs alone.<sup>31</sup> Cyanosis is the most specific clinical correlate of arterial

oxygen saturation, but it is shown to be an unreliable predictor of moderate hypoxemia and is difficult to detect in highly pigmented skin types and in children who are anemic. Hypoxemia is the single greatest risk factor for pneumonia-related death.<sup>27</sup> Hypoxemia is also a predictor of poor outcome in children with other diseases such as sepsis, severe malaria, meningitis, malnutrition, and asthma.<sup>32</sup>

In addition to the oxygen saturation readout produced by a pulse oximeter, other clinically important variables, such as RR,<sup>33</sup> heart rate variability, ΔPOP,<sup>19</sup> and CRT (extractable through advanced processing of the PPG), can be very useful in the detection of pneumonia and pneumonia-related sepsis, and in following the response to therapy.<sup>34</sup> Not only is pulse oximetry important for diagnosing pneumonia, but is also vitally important for real-time detection of treatment failure. If oxygen saturation levels do not recover within 24 to 48 hours of initiating treatment, the current treatment regimen should be considered insufficient.<sup>35</sup> Another key use of pulse oximetry is the titration of oxygen administration. Use of oxygen to manage pneumonia can reduce pneumonia-related fatalities by >35%.<sup>36</sup> However, the logistics and prohibitive cost of maintaining reliable oxygen supplies in the developing world challenge the delivery of this life-saving treatment. This is compounded by the lack of appropriate diagnostic tests and pulse oximetry devices to initialize and prioritize the allocation of oxygen resources.<sup>37</sup>

**PULSE OXIMETRY FOR THE PREDICTION OF COMPLICATIONS FOR PREECLAMPSIA IN PREGNANCY**

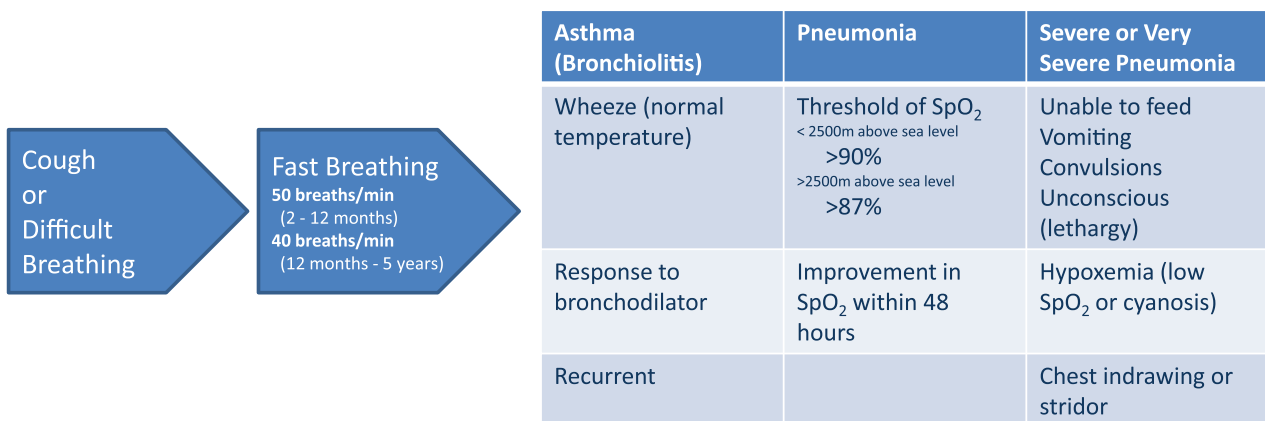
Globally, preeclampsia is the second leading cause of maternal mortality, resulting in an estimated 76,000 maternal deaths annually. In addition, 500,000 fetal and newborn lives are lost annually due to the perinatal consequences of preeclampsia. More than 99% of these deaths occur in low- and middle-income countries, primarily in South Asia and sub-Saharan Africa.<sup>38</sup> While expectant management of women with preeclampsia may improve perinatal outcome, the definite treatment is delivery.

Reducing the devastating maternal consequences of preeclampsia, such as convulsions, stroke, and ultimately death, is dependent on the ability to predict which women will develop complications, a clinical challenge in mothers

with preeclampsia. Many women with preeclampsia lack clinical warning signs, and the complications can be life threatening, even when arterial blood pressure increases are mild.<sup>39</sup> A preeclampsia survey in the United Kingdom (1994) showed that 11% of women presenting with an eclamptic convulsion had neither hypertension nor proteinuria, and 85% of women had been seen within 7 days before the onset of eclampsia. Similarly, the “Confidential Enquiry into Maternal Deaths” in the United Kingdom showed that the cases of fulminate preeclampsia resulting in maternal mortality all occurred within 7 days of an unremarkable routine antenatal visit.<sup>40</sup> This reflects the inability of conventional antenatal care to reliably detect severe preeclampsia or impending eclampsia.

Recently, oxygen saturation was identified as a novel and powerful independent clinical predictor of adverse maternal outcome, with oxygen saturation <93% identified as a threshold associated with a particularly high risk of adverse outcomes.<sup>41</sup> Preeclampsia, more than proteinuric gestational hypertension alone, is a state of exaggerated systemic inflammation. Maternal morbidity and mortality due to preeclampsia relate to both uncontrolled hypertension and the pulmonary and hepatic consequences of systemic inflammation.<sup>42</sup> The low oxygen saturation should then not be an unexpected finding in the setting of systemic inflammation.

Pulse oximetry is included in the recently validated Preeclampsia Integrated Estimate of RiSk (PIERS) model<sup>43</sup> for predicting complications of preeclampsia. The PIERS model was able to accurately stratify women into risk categories (based on *n* = 1534) and predicted adverse maternal outcomes within 48 hours of study eligibility (area under the receiver operating characteristic curve 0.88, 95% confidence interval, 0.84–0.92), and even up to 1 week (area under the receiver operating characteristic curve >0.7) after enrollment. The prediction includes pulse oximetry, gestational age, chest pain/dyspnea, serum creatinine, platelet count, and aspartate transaminase. The PIERS model attains similar stratification capacity, calibration ability, and classification accuracy as established cardiovascular<sup>44</sup> and critical care scores.<sup>45</sup> The group with pulse oximeter oxygen saturation (SpO<sub>2</sub>) between 90% and 93% had an odds ratio of 18.1 (95% Confidence Interval, 8.2–40.2) for all outcomes within 48 hours.<sup>41</sup>



**Figure 3.** Community level diagnosis of pneumonia in the sick child aged 2 months to 5 years of age. SpO<sub>2</sub> = pulse oximeter oxygen saturation.

Table 2. Challenges in the Development of Camera Oximetry		
Component	Challenge	Detail
Camera sensor	Selection of region of interest impacts calibration factor	Variations in focal plane result in variations in number of photons reaching each pixel
	Dynamic range limited	Different path lengths at different regions
	Color sensitivity is optimized for the human eye	Limited to 8 bits per color channel or 24 bits per pixel
	Quantum efficiency of the sensor dependent on wavelength	More green pixels may result in a sensitivity bias toward the green spectrum
	White balance	Requires knowledge of emission spectrum of light source
	Larger field of view compared with photodiodes	Algorithms are unknown and limit bandwidth
	Limited sampling rate	Increased risk of optical shunt
Light source	Infrared notch filter	30 frames per second unless a reduction in image resolution
	Unstable emission spectrum	Used to reduce glare in consumer cameras; limits use of infrared spectrum for oximetry
Phone	Broad emission spectrum	Light-emitting diodes used in the camera flash have temperature-dependent emission spectra
	Hardware fragmentation	Increased risk of optical shunt
	Build quality	Hardware varies strongly between models requiring particular calibration The quality of consumer goods manufacturing may be low; variability between devices

The implementation of this predictive score in the clinical environment is challenging and would require a readily available computing device that can combine the PIERS model with vital sign measurements like pulse oximetry. The prohibitive costs and limited availability of diagnostic tests and medical devices are a barrier to the widespread use of this model in low-resource settings, where it would be most impactful.

**MOBILE COMPUTING DEVICES AS MONITORS**

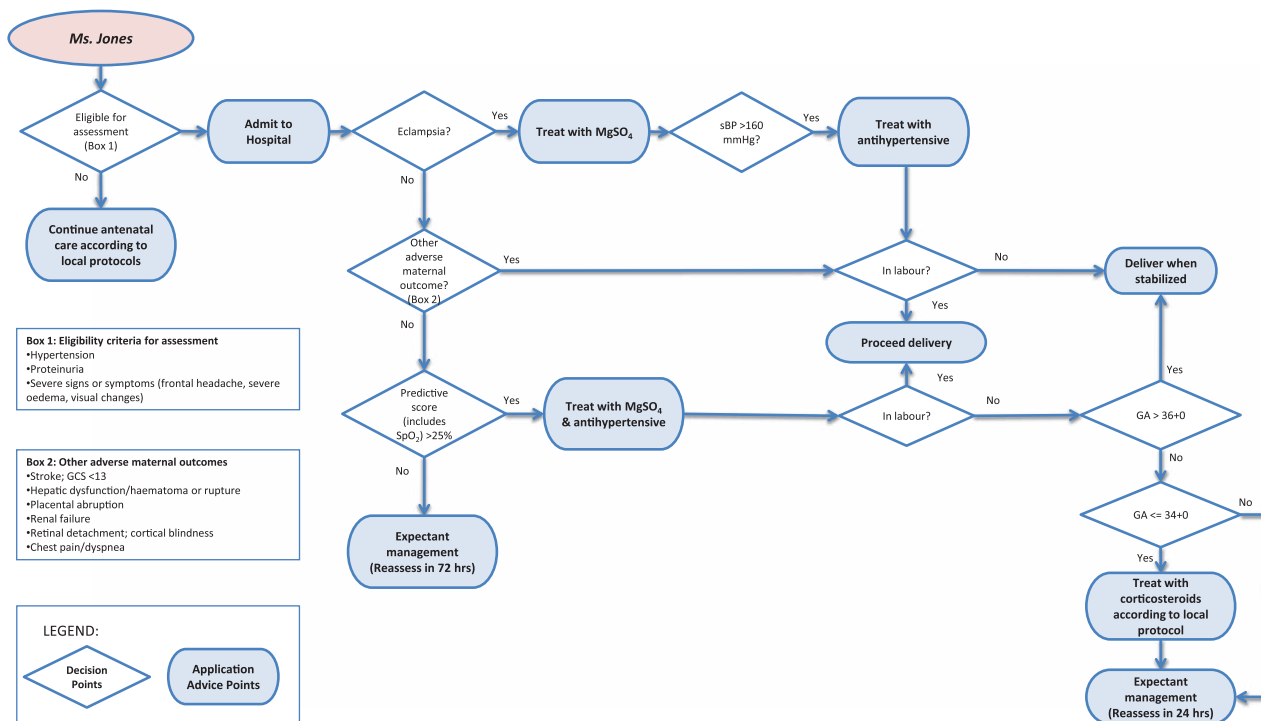
An alternative and relatively new approach to overcoming device availability in many clinical settings may be to use devices such as cell phones or computers, already available in these locations, as monitors. The inherent computing power of these devices and their everyday availability offer the opportunity to create a stand-alone device that can be used in the home by patients, yet which can also communicate with clinicians in real time. Previously owned devices can also be repurposed as monitors in resource-poor areas of the world.

Pulse oximetry modules from commercial manufacturers that can communicate with a mobile device have been clinically evaluated for anesthesia<sup>46</sup> and are undergoing clinical trials as spot-check diagnostic devices for preeclampsia and childhood sepsis prediction (unpublished data). A pulse oximetry module for the iPhone for nonmedical use is now commercially available (Table 1, Ref. 7). The mobile device is only used as a display and power source in these applications while the majority of the processing is performed on the cable microcontroller. To realize the potential for affordable sensors, the processing should ideally be performed on the mobile device. A solution has been proposed to use the sound card, via the standard audio jack, to process the signal from the pulse oximetry sensor.<sup>47</sup> A conventional oximeter finger sensor is interfaced to the phone via the headset jack by fitting it with a 3.5-mm tip-ring-ring-sleeve connector that plugs directly into the phone. The sensor light-emitting diodes are driven by the speaker output. The diodes were wired in reverse polarity, which facilitates activating the diodes at opposite polarities to the driving signal. And the sensor photodiode generates a voltage in response to the

transmitted light. This signal is compatible with the microphone input of the audio channel and can be detected without amplification or conditioning. It was, however, found beneficial to boost the signal amplitude with a single field-effect transistor powered by the microphone bias signal. The ultimate inexpensive solution would be to use the phone camera as the sensor and to perform processing on the mobile device. The current camera technology has a number



**Figure 4.** An example of a sensor attached to a mobile phone for pulse oximetry monitoring. This application is called the Phone Oximeter. The sensor is attached to the phone using the power port of the device.



**Figure 5.** Decision tree showing possible decision and advice points that could be used with a predictive score such as the Pre-eclampsia Integrated Estimate of RiSk (PIERS) score (derived from pulse oximetry, gestational age, chest pain/dyspnea, serum creatinine, platelet count, and aspartate transaminase). The pulse oximeter oxygen saturation (SpO<sub>2</sub>) measured on the mobile device could be combined with other relevant clinical information to guide clinical care. MgSO<sub>4</sub> = magnesium sulfate; sBP = systolic blood pressure; GCS = Glasgow Coma Scale; GA = gestational age.

of limitations such as the types of camera sensors used and filters that remove desirable wavelengths of light (Table 2).<sup>48</sup>

A number of significant barriers need to be overcome to make mobile devices a viable alternative for vital sign monitors. These include a universal method to connect sensors to devices, as well as procedures to ensure the reliability of measured variables. The battery life and size of a cell phone display may not meet the requirements for some clinical applications, such as continuous monitoring during anesthesia. However, their portability make them ideally suited for use as spot-check devices.

The powerful and inexpensive mobile application development and distribution environment offer the opportunity to develop and deliver a range of applications to support sensors, such as those for pulse oximetry, attached to a mobile device (Fig. 4).<sup>46</sup> This will deliver the promise of pulse oximetry combined with supportive diagnostic and treatment applications into every medical setting and every home. For example, PIERS on the Move is an application that combines the PIERS model and pulse oximetry on a mobile device (Table 1, Ref. 8). This complex decision model is encapsulated in a mobile application that provides real-time advice to the user who is unaware of the complexity of the decision (Fig. 5). Communication channels offered by the mobile device will leverage social interaction and media to engage patients and health care providers in new models of health care delivery.

**CONCLUSION**

The universal availability of mobile devices offers a computing device, power source, and display to which we

can attach a wide variety of physiological sensors. This can include noninvasive measurements of electrocardiography (AliveCor, Inc., San Francisco, CA), electroencephalography, oxygen saturation,<sup>46</sup> hemoglobin, glucose, arterial blood pressure, spirometry (Table 1, Ref. 9), temperature, energy expenditure, weight, and height. Even the built-in sensors of the phone can be used to measure vital signs; for example, the accelerometer can be used to measure respiratory activity, and the camera can be used to measure heart rate and RR.<sup>46</sup> Innovative use of the information from these sensors will see a surge in new software applications, further leveraging the communication capability of the mobile device.

Mobile phones can also be used to contact or be contacted, as an information resource to guide care, as an explanation resource for patients, deliver e-learning for providers, as a logbook for reflective learning, and for teleconsultation and remote support.<sup>49</sup> The widespread availability of pulse oximetry on mobile devices will realize the potential of pulse oximetry as both a monitoring and diagnostic tool in a wide range of clinical settings. Oxygen saturation will truly become recognized as one of the vital signs. ■■

**DISCLOSURES**

**Name:** J. Mark Ansermino, MBCh, FRCPC.  
**Contribution:** This author designed the Special Article, searched the literature, and wrote the manuscript.  
**Attestation:** J. Mark Ansermino approved the final manuscript.  
**This manuscript was handled by:** Dwayne R. Westenskow, PhD.

**Conflict of Interest:** J. Mark Ansermino has been a paid consultant to GE Medical and is a founder and director of LionsGate Technology, a medical devices startup.

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