Letters to the Editor

Pulse Oximeters Are Not Racist

As the Founder and CEO of Masimo, I co-invented the modern-day measure-through motion and low perfusion pulse oximeter (SET® Pulse Oximeter) and have spent my life in pursuit of data-based solutions throughout healthcare, most prominently in monitoring patients via pulse oximetry.

The December 17, 2020 *New England Journal of Medicine* article, "Racial Bias in Pulse Oximetry Measurement," is correct that black patients have been a challenge for conventional pulse oximetry, resulting in the overestimation of arterial blood oxygen saturation. When I started Masimo in 1989, this is a variable we worked to address with our SET® Pulse Oximeter by making sure to have an equal number of dark-skinned and light-skinned people represented in our calibration studies. However, I do not believe that the whole picture has been painted here, leaving room for some to create an inaccurate narrative with potentially lethal consequences.

"When I started Masimo in 1989, this is a variable we worked to address with our SET® Pulse Oximeter by making sure to have an equal number of dark-skinned and light-skinned people represented in our calibration studies."

For context, multiple studies over the years have examined this issue and reported a bias between -1.6% to +3.9% between different brands of pulse oximeters. A 2017 study of infants with hypoxemia comparing Masimo and Medtronic pulse oximeters found an overall bias with black infants of 0.8% for Masimo devices and 3.9% for Medtronic devices.(1) The authors concluded at the time that there was "no significant difference in systematic bias based on skin pigment for either oximeter."

Given that the University of Michigan study, published as a letter to the editor in *The New England Journal of Medicine*, had many more subjects than the previous studies, I wondered if maybe we had not noticed the bias because the sample sizes in the previous studies were smaller. Therefore, we did a further review of our internal data—which covers over 2,000 subjects with more than 1,000 dark-skinned people (more than the number of subjects in the Michigan study)—and found a 0.3% difference between the groups across an oxygen saturation range of 70-100%, and a 0.25% in the more limited pulse oximetry range the Michigan study focused on. Applying the statistical test used in the Michigan letter to our internal data, we found a difference between dark and light-skinned subjects of 1%, whereas that same test applied in the Michigan study found a 325% difference.

Although we recorded skin color for all of the subjects in our validation dataset (using the Massey-Martin pigmentation scale), most subjects did not report ethnicity. To expand our analysis, we also compared just those black and white subjects who *had* reported ethnicity—394 subjects, 200 black and 194 Caucasian, a similar ratio as in our overall dataset—and found a similar bias, 0.4%, between the two groups.

Given that our bias was so much less than that of the Michigan study, we questioned what could be the cause of the disparity between the results presented by the University of Michigan authors and all the data we had seen in the past two decades?

We came up with several hypotheses, and here are some of them:

Sickle-cell disease is one potential confounder. The sickle-cell trait affects nearly 10% of the black population. Sickle-cell disease has been shown to cause significant errors between invasive CO-Oximeter and noninvasive pulse oximeter measurements.(2) If sickle-cell patients were not excluded in the Michigan study, that alone could account for most of the difference between what we have seen and what Michigan reported. The question is, did the Michigan study account for this?

"MetHb not only causes huge errors in pulse oximetry, including biasing pulse oximetry readings but also can kill the patient if it's not detected and treated immediately.(6) Did the Michigan study account for this?"

An additional error source for pulse oximetry is the presence of high carboxyhemoglobin (COHb) and methemoglobin (MetHb) in the blood. (3, 4) The Michigan researchers briefly discussed COHb but did not discuss if they excluded patients with high MetHb. There are over 40 drugs commonly given in hospitals that unfortunately can elevate MetHb to dangerous levels. One of them, hydroxychloroquine (which has been recently used on COVID-19 patients), has been shown to elevate MetHb in black patients dramatically. (5) MetHb not only causes huge errors in pulse oximetry, including biasing pulse oximetry readings but also can kill the patient if it's not detected and treated immediately.(6) Did the Michigan study account for this?

Another confounder could be tissue damage and poor circulation, which afflicts black people more than any other racial or ethnic group and can also negatively affect the accuracy of the pulse oximetry readings. (7, 8) So again, did the Michigan study account for this?

In addition, to speak of pulse oximeters as though they are all the same in accuracy and reliability is wrong. While the University of Michigan has been our customer for many years, and we have to assume the pulse oximeters they used in their study are ours, we are not certain that they were. It is important that researchers report the brand and version of the pulse oximeters and sensors they used. For example, the data shown in Figure 1 in the Michigan study exhibit a very large spread, which is inconsistent with many independent peer-reviewed studies of Masimo SET® pulse oximeter accuracy over the past decades.(9) These inaccuracies are usually associated with conventional pulse oximeters, or worse, the cheap knock-off finger-clip pulse oximeters that are sold at local pharmacies.

Another confounder is the unacceptably large delay between pulse oximetry readings and invasive blood sampling, during which a patient's oxygen saturation may be changing. In our internal studies, care is taken to record pulse oximetry measurements simultaneously with invasive blood samples. The Michigan study did not have that critical control, and up to 10 minutes passed between the two measurements—even though the oxygen saturation of sick patients can change dramatically in 10 seconds.

While I do not know if these potential sources of error are the confounders that created such a large bias between black and white patients in the Michigan study, I do believe that the Michigan study should prompt further investigations, with the goal of removing systematic sources of error from the data collection to uncover any true source of pulse oximetry bias.

What these publications did is regretful:

- With very little explanation and underlying data, the Michigan authors sent in their findings.
- The *New England Journal of Medicine* published *their* findings seemingly without asking for the kind of data that you expect in a scientific journal.
- The *Boston Review* and the *New York Times* rushed to give the purported bias in a pulse oximeter a racist narrative.

We need to go back to our meritocracy and not let the acts of some badly behaved people change who we are. Yes, we have a race issue in our country—one that I believe we, as individual citizens, need to do everything in our power to fix. My family and I, along with our friends and colleagues, marched for Black Lives Matter. We seek opportunities to stand up for justice and peace everywhere we can. We join every other citizen who understands the brilliance of action out of kindness. When it comes to developing products and running our company, we stick with data and science done by the best people, no matter their beliefs, race, sex, or sexual orientation.

In the pursuit of science and patient safety, we will further test our hypotheses about the source of the high pulse oximetry bias on black patients in the Michigan study and will report our findings in the near future. We have been in touch with the Michigan researchers and hope to work with them as well as any other committed researchers toward helping to ensure the health and safety of ALL humankind.

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Thank you and kind regards,

Joe Kiani

Founder and CEO, Masimo

This manuscript was originally published in the Orange County Business Journal, reprinted with permission.

Dear Mr. Kiani

The concept that a technology as vital as pulse oximeter could be racist is beyond comprehension. Although darker skin pigmentation may present more challenges, the medical device industry is a challenging space. There are tight, at times overwhelming regulations, a requirement for superior accuracy, and a steep curve to achieve clinical relevancy. It is unusual and disruptive when a company comes to market with a technology that fundamentally changes the way clinical outcomes are measured (1).

However, such was the case in 1989, when Joe (Masi) Kiani and Mohammed (Mo) Diab set out to build a better pulse oximeter, a device that measures oxygen saturation in blood non-invasively. Both were electrical engineers who had previously worked with early models of pulse oximetry that employed conventional measurement technology to assess these values (2). In certain patients, these devices were unreliable. Where there were high motion and low perfusion, the oximeters became less reliable, leading to the inappropriate titration of oxygen and other therapeutic misadventures. Working out of Mr. Kiani's garage, Masimo came together. As opposed to working from a top-down perspective and striving for incremental improvements in standard metrics, Masimo strove to revolutionize the way oximetry was measured (2). Conventional oximetry works by measuring a "ratio of ratios," comparing the moving components of red light to nonmoving components in the numerator to the moving components of infrared light to nonmoving components in the denominator. Motion causes an additional signal to be present in both the numerator and the denominator, overwhelming oxygen saturation measurement. Poor perfusion decreases the amplitude of both the numerator and denominator to the point that the signal because hard to read. Darker pigmentation affects light absorption. Without appropriate calibration for skin coloration, improvements in a technology that read through motion and low perfusion would be limited at best. With their training in algorithms and mathematical modeling, Masimo used these technological implementations to improve upon conventional oximetry and introduce real-time modeling of physiological change.

In the early 1990s, the technology was ready for clinical testing. However, when Masimo approached clinicians, they found that many of these clinicians regarded this innovation as a technology in search of a problem. Pulse oximetry was considered a mature technology. In well adults and children, pulse oximetry worked "good enough" to provide an estimate of clinical wellbeing. By many, it was referred to as a "fair weather" friend. Not thought to be as robust or accurate as invasive blood monitoring of oxygen levels, physicians, in particular, regarded this technology as one that provided an adjunct to care (2). Working through extensive contacts, Masimo continued to approach clinicians about doing studies using this novel signal extraction technology or SET in their patients. One physician presented them with a unique challenge (3). As a trainee in Neonatal-Perinatal medicine at a local university medical center, he had seen the devastating effects of relying upon conventional pulse oximetry in these most at-risk babies. Pulse oximetry was unreliable in over 90% of these patients. Small preterm infants of every race were subject to oxygen concentrations that resulted in long-term eye problems

and even blindness (4). Some were kept on ventilators much longer because of concerns regarding whether they were getting adequate oxygen to provide growth and development. This "budding" neonatologist had called the oximeter company that provided the conventional oximetry technology to the hospital and was told, "You should be glad it works at all." The technology was not designed for monitoring small preterm babies regardless of their race and had not been validated for this use. What followed was research by this physician and others that demonstrated the importance of SET in these patients. In numerous studies, it was shown to be superior to conventional oximetry (2). Not only did the technology read through motion, low perfusion with more accuracy than thought possible but it also read through different pigmentations. Neonates are not only difficult to monitor because of their physiology but because of the changes in their pigmentation. Over the course of these initial studies, Masimo algorithms were adapted not only to skin parameters immediately after birth but also to changes that occurred over days and weeks that followed. The attention to detail was not based on what was expedient but what was right for those neonates most at risk. Indeed, the initial prototype oximeters were referred to as the "Stork."

At this point, the technology was software only. Masimo had to find medical device manufacturers in the hardware space who would install their software and use it in their installations. By not having to support a hardware base, Masimo figured that it would focus its efforts on the technological end and rely on other more established organizations to provide the distribution network.

What they found was very much different from what they had hoped for in their initial marketing efforts. Manufacturers of conventional oximetry were not interested in their technology. They took exception to the thought that the software product produced by this start-up could improve upon their offerings. They commissioned competing studies and argued that SET's technological improvements including those that addressed the issue of darker pigmentation were only applicable in special circumstances. Some signed non-disclosure agreements but then, despite initial praise of the benefits, rejected the technology as one that did not meet their specifications for various reasons. One day, one of the competing firms called Joe Kiani and offered him a million dollars for exclusive technology rights. The sum would have covered most of the corporation's increasing debt and would have potentially allowed Masimo technology to be used in subsequent products made by the competitor. Mr. Kiani vetted the proposal to several clinicians, including some of his original advocates. The competitor was trying to acquire the technology in order to "shelf" it. The investigation into the other competitors' acquired technologies demonstrated that they were not ultimately developed into products to improve patient outcomes. In situations where an existing manufacturing facility was acquired, the plant was closed within a short period of time. It was more profitable for this competitor to market using their existing patents and kill innovative technology to challenge the *status quo*. Patient outcomes were secondary to profit. Mr. Kiani turned the offer down (1, 2).

Not having a hardware base impeded further progress. Further improvements in software were technology and sensor-specific. The conventional oximeters and their Masimo had outgrown the original target. They would ultimately have to manufacture a hardware device and transition from a company that provided a software component to a medical device manufacturer. Masimo cared enough to do the right thing even when it would have been expedient to pursue a different path.

Over the intervening years, the technology received considerable attention; not only was Masimo able to demonstrate improved accuracy, precision, and outcomes in all patients, but the use of the equipment had actually saved the life of a newborn with complex congenital heart disease (2, 5). Masimo technology could measure not only those patients who were subject to routine neonatal problems but also those at *extremis* and most at risk of disparity. Masimo did not take shortcuts, it did not develop a technology that worked only for adults or only those individuals with lighter skin. Masimo looked first at the most challenging problems in neonates before moving on to older patients. On the strengths of these metrics, Masimo rose to the challenge and monitored though motion, perfusion and disparity (1). For Masimo, Black Lives have always mattered.

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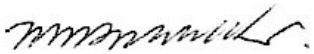
Sincerely,



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