Carboxyhemoglobin (COHb) Clinical Spotlight

Performance and Reliability of Nonin COHb Technology

Count on Nonin.

About Nonin Medical

Since 1986, Nonin Medical has developed reliable technologies and manufactured durable noninvasive patient monitoring devices for healthcare professionals and consumers. Nonin pulse oximeters, cerebral and tissue oximeters, capnographs, sensors, and software deliver dependable performance day after day—even in challenging environments.

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The studies presented in this monograph were performed with investigational devices and with IRB approval. The study results have been previously presented at international professional society meetings, the details of which appear at the end of each study summary.

Reasons to Monitor COHb

Carbon Monoxide Poisoning

Carbon monoxide (CO) is an odorless, colorless gas generated from incomplete combustion and is one of the most important international causes of toxicological morbidity and mortality.[1] In 2012 the World Health Organization reported that Europe had an annual death rate of 2.2 per 100,000 people from CO poisoning. This CO mortality rate can be compared to the mortality rates for HIV/AIDS, skin cancer or alcohol abuse (2.0, 2.1 and 2.6 per 100k people respectively), all of which have been regarded as public health issues. In some countries such as Estonia and Belarus (11.99 and 6.2 per 100k people) mortality rates can even be compared to diabetes at 11.4 per 100k people.[2]

In contrast the United States (US), England, Germany and France experience lower mortality rates (see table 1) but instead have higher rates of diagnosis and hospitalization, with the US alone having an estimated 50,000 CO poisoning cases each year.[3] These differences are due to a number of factors including established programs for diagnosing and reporting on CO poisoning.[2] For example, recognizing the danger CO poses, the US National Fire Protection Association recommends assessing firefighters after any potential exposure.[4] Similar measures have been recommended in the United Kingdom to address this growing issue.[5] Ultimately, the biggest impact on the healthcare system is the high incidence of EMS provider calls, which increases globally in the winter months,[2, 6-8] and the significant risk of delayed or missed diagnosis.[9-13]

Table 1: Rates for Carbon Monoxide Mortality, Hospital Admission, and Annual ED visits (per 100k people). Rates are for total admissions not excluding fire or suicide.

Country	Annual Death Rate	Hospital Admission Rate	Annual Emergency Visits
United States	0.96	1.52	16.61
Europe	2.24	2.3	
England	0.32	1.07	7.07
Germany	1.9	3.59	5.4
France	0.69	2.12	13.66

Point of Care Measurement

CO poisoning is difficult to diagnose because few effective point of care tools exist to identify the presence of CO in the blood and exposure usually remains undetected until injury or death.[18, 19] CO binds to hemoglobin in the blood producing carboxyhemoglobin (COHb). COHb replaces oxygen, causing systemic hypoxemia.[1] Traditionally, pulse oximeters have been used for point of care blood gas exchange monitoring. However, they are unable to detect COHb and produce an overestimation of the arterial blood oxygenation when COHb is present.[20-22] Conventional medical care uses observation of clinical signs and symptoms to determine CO exposure severity and diagnose poisoning.[23] However, CO poisoning can produce a variety of clinical effects that resemble other neurological, cardiovascular, and systemic disease conditions, leading

to potential misdiagnosis.[9-13] Moreover, recent work has shown that signs and symptoms do not correlate to blood COHb levels for assessing exposure severity.[11, 12, 24]

Recent scientific advances have enabled pulse oximetry that can measure COHb.[25] Until now, this pulse oximetry technology (Masimo, Irvine CA) has been the only noninvasive point-of-care tool capable of measuring COHb, but researchers have seen an extensive "discordance of results reported in the available literature"[26] and concluded that "based on the available clinical data, there is insufficient evidence for its broad clinical use".[27] The American Academy of Emergency Physicians added its recommendation in 2017 that Emergency Departments not "use noninvasive COHb measurement (pulse CO-oximetry) to diagnose CO toxicity in patients with suspected acute CO poisoning."[28] In review of the available literature the current technology struggles to produce COHb readings in the presence of hypoxia[29] and has a false negative rate of ~50% (at a clinical threshold of 10% COHb) during spot-checking and continuous monitoring.[29-31] Therefore, "further work to develop an accurate, precise, user-friendly, and noninvasive COHb monitoring is warranted"[27], and "rapid, noninvasive means of accurately measuring blood COHb levels could offer numerous benefits" for emergency department and out-of-hospital patient care.[26]

Emerging Technology

Nonin Medical has developed a new multi-parameter oximetry system (CO-Pilot™ Wireless Handheld Multi-Parameter Oximetry System (H500)) with technology capable of accurately measuring COHb (A_{RMS} <3.0%) through concurrent hypoxia. This new system solves other clinical issues as well by generating 80% fewer false negatives than the current standard when used for spot-checking. In addition, the system produces accurate SpO_2 readings even in the presence of elevated COHb, a feature desired by emergency medicine clinicians but not available with today's noninvasive COHb monitoring.

Note: The studies reviewed in this clinical monograph were performed using a non-commercial version of this technology referred to throughout this document as the SenSmart® Multi-Sensing Oximetry System.

Calibration/Validation Study of the Nonin SenSmart® Multi-Sensing Oximetry System to Measure Arterial Oxygen Saturation during Carboxyhemoglobinemia

David MacLeod[1], Zachary Augustine[1], Maria Santoro[1], Aaron Lobbestael[2]

Key Takeaway

The Nonin SenSmart® Multi-Sensing Oximetry System produces reliable SpO_2 readings even in the presence of elevated COHb, and conversely, produces reliable COHb readings even in the presence of low SpO_2 saturations.

Study Summary

The objective of this study was to calibrate and validate the accuracy of Nonin SenSmart® Multi-Sensing Oximetry System SpO_2 and COHb measurements at multiple intervals during elevated COHb up to 15%, and SpO_2-measured hypoxia down to 80%.

Study Design

Thirty-six healthy volunteers (19M; 17F) were recruited to a single center, prospective, non-blinded, randomized study. Two subjects were withdrawn due to difficult arterial line placement. The SpO_2 and COHb data from subjects 1–24 was used to calibrate the oximetry system; data from subjects 25–34 was used for validation. Each subject completed a series of controlled, incremental oxygen desaturations over the range of 70–100% in the presence of variable COHb over the range of 0–15%, administered by inhalation of CO gas mixture. Serial arterial blood gas (ABG) samples were drawn at each step and processed with a Radiometer ABL90 co-oximeter to measure SaCOHb and functional blood oxygen saturation (SaO_2). The A_{RMS} of COHb and SpO_2 with and without concurrent elevated COHb were calculated. A_{RMS} is reported with the [95% confidence interval]. Bland-Altman analysis was also performed for SpO_2 with and without elevated COHb.

Key Results

Thirty-four subjects completed the study with a total of 1,236 ABG samples drawn. The accuracy of the %COHb measurement was similar with (A_{RMS} 2.6 [2.28, 3.22]) and without (A_{RMS} 2.5 [2.19, 3.15]) concurrent hypoxia. During hypoxia without concurrent elevated COHb (<3%) the A_{RMS} of SpO_2 over the SaO_2 range of 70–100% was 1.5% [1.34%, 1.81%]. Elevated COHb (0-15% COHb) did not degrade the accuracy of the SpO_2 measurement (A_{RMS} 1.4% [1.25%, 1.51%]). The slope (COHb<3%:0.02, COHb0-15%: 0.02) and intercept (COHb<3%:-1.92, COHb0-15%: -1.21) of the Bland-Altman analysis was not affected by the presences of elevated COHb.

Conclusions

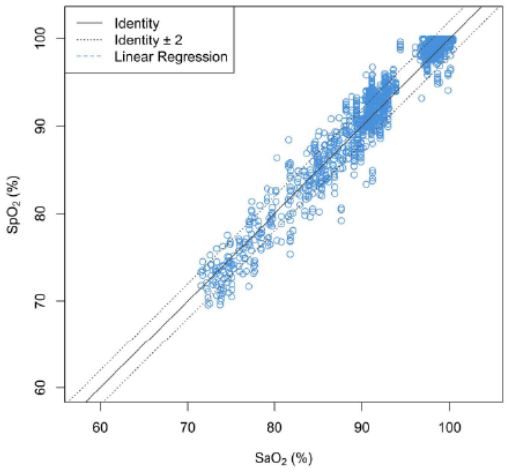
The Nonin SenSmart Multi-Sensing Oximetry System provided accurate measurements of SpO_2 throughout the range 70–100% and during elevated COHb up to 15% in healthy volunteers. The system provided accurate COHb values both with and without concurrent hypoxia. This new monitoring tool will enable pre-hospital and ER staff to monitor and assess the health of patients throughout transport for CO poisoning, potentially mitigating the severity of hypoxia events.

[1]Duke Human Pharmacology & Physiology Lab, Durham, NC, USA
[2]Nonin Medical Inc, Plymouth, MN, USA

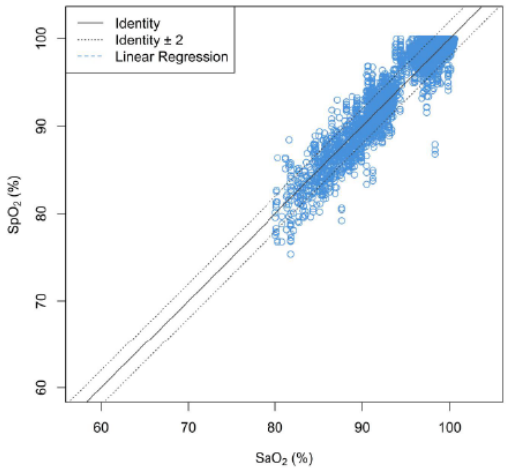
Presented at the 2018 American College of Emergency Physicians Scientific Assemble (ACEP)

San Diego, California

SpO_2 accuracy claim is 2.0 A_{RMS} as presented in the charts below.

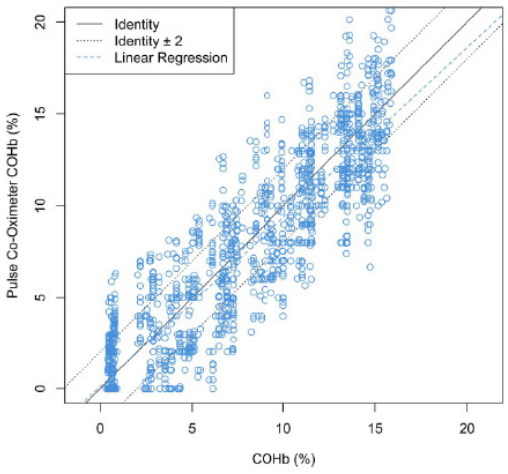


SaO_2 Range	COHb Range	A_{RMS} (95% CI)
70–100%	0–3%	1.5 (1.34, 1.81)

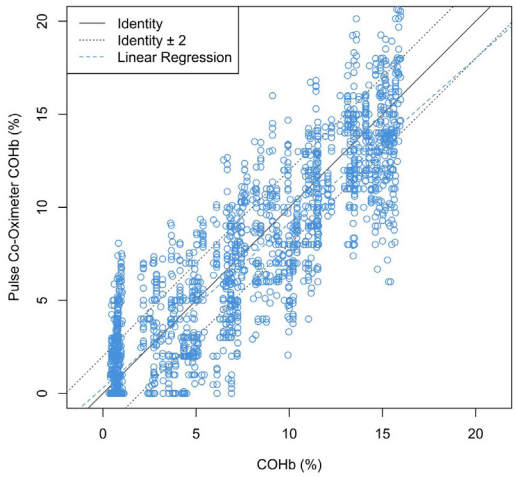


SaO_2 Range	COHb Range	A_{RMS} (95% CI)
80–100%	0-15%	1.4 (1.25, 1.51)

COHb accuracy claim is 3.0 A_{RMS} as presented in the charts below.



SaO_2 Range	COHb Range	A_{RMS} (95% CI)
95–100%	0–15%	2.5(2.19, 3.15)



SaO_2 Range	COHb Range	A_{RMS} (95% CI)
80–100%	0–15%	2.6(2.28, 3.22)

Accurate Carboxyhemoglobin Spot-Check with a New Pulse Oximeter in the Presence of Hypoxemia

David MacLeod[1], Marcus Kramer PhD[1]

Key Takeaway

The Nonin SenSmart® Multi-Sensing Oximetry System produces reliable and accurate sensitivity and specificity during a COHb spot-check application. It accurately measures COHb during spot-checking and especially in the presence of hypoxemia.

Study Summary

The objective of this study was to evaluate the spot-check accuracy of a new noninvasive system for measuring COHb.

Study Design

Following IRB approval, consent and screening, healthy volunteers were recruited for a prospective, non-blinded, randomized study. Each subject received incremental doses of CO (COHb range of 0–15%) with concurrent desaturations (SaO_2 range of 80–100%) controlled by inhalation gas mixtures. Stable gas plateaus were held for ABG sample collection and evaluation (ABL90, Radiometer). During the plateaus, multiple COHb noninvasive sensors (SenSmart Multi-Sensing Oximetry System, Nonin Medical) were exchanged at 60-second intervals on the non-arterial hand to replicate a spot-check use case. Spot-check performance was measured using the accuracy root mean square difference (A_{RMS} 95% confidence interval), sensitivity and specificity comparing arterial and noninvasive COHb estimates.

Key Results

Ten subjects (7M, Age: 30±10, BMI: 25±3 Kg/m2) completed the study with a total of 169 blood samples drawn. The A_{RMS} of COHb spot-checking during CO exposure and normoxia was 2.2% [1.94%, 2.45%]. Concurrent hypoxia didn't significantly degrade the COHb measurement, producing an A_{RMS} of 2.5% [2.28%, 2.75%]. CO exposure greater than 10% clinical threshold were detected with a sensitivity of 89.40% and specificity of 93.08%.

Conclusions

These results demonstrate a satisfactory accuracy, sensitivity and specificity for the noninvasive system studied, used in a COHb spot-check application. The ability to accurately measure COHb during spot-checking, and especially in the presence of hypoxemia, represents a significant technical improvement for medical professionals to help triage patients.

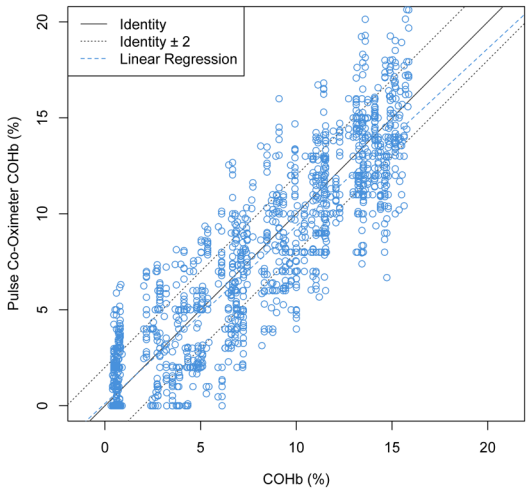
[1]Duke Human Pharmacology & Physiology Lab, Durham, NC, USA
[2]Nonin Medical Inc, Plymouth, MN, USA

Presented at the 2019 National Association of EMS Physicians (NAEMSP) Annual Meeting

Austin, Texas

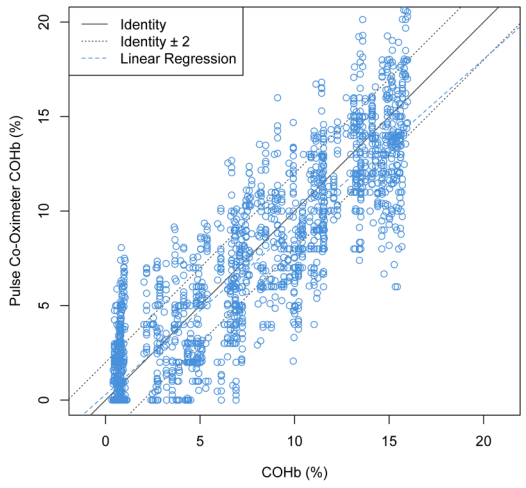
%COHb Accuracy Results for the Nonin Multi-Sensing Oximetry System during Non-Hypoxic Conditions (SaO_2 95-100%) with Induced Carboxyhemoglobinemia

A_{RMS} (Bias Corrected Adjustment)	
0-15% COHb	2.2 (1.94, 2.45)
0-5% COHb	1.9 (1.64, 2.21)
5-10% COHb	2.4 (2.03, 2.89)
10-15% COHb	2.4 (2.05, 2.59)



%COHb Accuracy Results for the Nonin Multi-Sensing Oximetry System during Hypoxic Conditions (SaO_2 80-100%) with Induced Carboxyhemoglobinemia

A_{RMS} (Bias Corrected Adjustment)	
0-15% COHb	2.5 (2.28, 2.75)
0-5% COHb	2.2 (1.85, 2.40)
5-10% COHb	2.7 (2.29, 3.03)
10-15% COHb	2.8 (2.51, 3.03_



Accuracy of Measuring Carbon Monoxide Poisoning with a Noninvasive Oximetry System Compared to Hospital Co-oximetry

Marcus Kramer PhD[1], Walter Holbein PhD[1]

Key Takeaway

In an ED environment on actual CO-poisoned patients, the Nonin SenSmart® Multi-Sensing Oximetry System delivered reliable COHb results that compared nicely with the hospital's invasive co-oximetry results.

Study Summary

The objective of this study was to demonstrate the accuracy of the COHb measurement as compared to invasive blood sample co-oximetry on suspected CO-poisoned patients in a hospital ED environment.

Study Design

The study was conducted in a NATO military hospital used as a referral center for CO-poisoned patients. During the study, blood samples (arterial: n=3; venous: n=17) were taken simultaneously with oximetry data. Blood samples were analyzed promptly by available hospital co-oximeters (Instrument Labs, Bedford, MA). Co-oximeter COHb values were compared to noninvasive COHb from the SenSmart Multi-Sensing Oximetry System (Nonin Medical, Plymouth, MN). The mean and standard deviations for both measurements and bias for COHb measurements from the co-oximeter and the noninvasive sensor (Model 8330AA) are presented. Lastly, the accuracy root mean square difference (A_{RMS}) between the noninvasive oximetry system and co-oximeter is presented.

Key Results

Results indicate that in clinical practice, measured COHb levels were similar between the invasive co-oximetry (14.1 ± 4.7%, range 4-21% COHb) and noninvasive oximetry (13.0 ± 6.2%, range 2-20% COHb) systems. The overall bias of the pulse oximetry based COHb estimation was −1.4% ± 3.3% and the A_{RMS} was 3.5%.

Conclusions

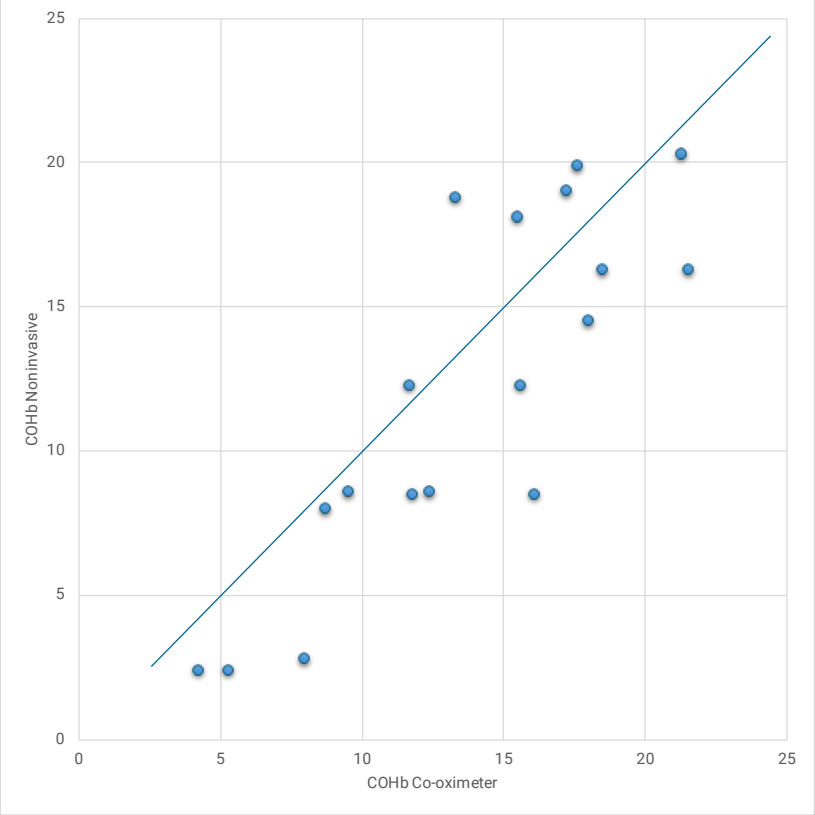
These results suggest the new SenSmart Multi-Sensing Oximetry System delivers high quality performance in an ED environment. This is in line with the manufacturer's specified accuracy of 3% in a more diverse population with more severe CO poisoning. The addition of the SenSmart Multi-Sensing Oximetry may significantly improve clinical decision-making by increasing confidence in the reliability of a quick, simple, pulse oximetry-derived COHb.

[1]Nonin Medical Inc, Plymouth, MN, USA

Presented at the 2018 European Society for Emergency Medicine Congress (EUSEM)

Glasgow, Scotland

Linear regression of Nonin's COHb measurement compared to invasive Co-oximetry.



Accuracy and bias across the carbon monoxide range, shown in the table below. Patient demographics: Two subjects removed from analysis due to high MetHb reading and no reportable noninvasive COHb.

Subject Demographics	
Category	**Subjects**
Subjects Removed	2/20
Age Range (Years)	16–96
Gender, n [%]	6/18
Skin Tone	
Light	7/18
Intermediate	8/18
Dark	1/18
Very Dark	1/18
Smoker, Yes	1/18

Monitoring for Carboxyhemoglobinemia During Fire Rehab with the Nonin CO-Met™ Noninvasive Oximetry System is Faster and More Reliable than the Masimo Rad-57

Keith Wesley, MD, FACEP, FAEMS[1]; Adam Valine NREMT, BS[1]

Key Takeaway

In a firefighter rehabilitation comparative trial, the Nonin SenSmart® Multi-Sensing Oximetry System was faster and more reliable in measuring COHb than the Masimo Rad-57® Pulse CO-Oximeter®.

Study Summary

The objective of this study was to evaluate the reliability of the COHb measurements from the Nonin device versus the Masimo device in actual firefighter rehabilitation.

Study Design

Firefighters undergoing standard fire rehabilitation during live burn training had a Masimo DCI sensor (with no light shield) connected to a Masimo Rad-57 Pulse CO-Oximeter placed on one hand per manufacturer's recommendation. On the opposite hand, a SenSmart 8330AA Multi-Sensing Fingerclip sensor was applied to the index, middle, or ring finger. Patient demographics were collected along with the noninvasive COHb, SpO_2, and pulse rate values obtained from both oximeters. Observations from the EMS personnel operating the two systems were also collected.

Key Results

Results include 59 measurements on 43 (42 M, 1F; Age 36 ± 10 years old, one smoker) enrolled firefighter patients. Longer fire events occasionally resulted in multiple rehabilitations and measurements for a single firefighter. The SenSmart Multi-Sensing Oximetry System reported readings for COHb on 100% of attempted measurements, whereas the Rad-57 had a blanked display on 25% of attempted measurements. Additionally, EMS operators noted that the Nonin device displayed readings faster than the Rad-57. 60% of blank readings on the Rad-57 occurred at a nighttime fire with an ambient temp of 18°F (−8°C). The Rad-57 manual notes that ambient light can interfere with its COHb readings. Light shields were not used with the Rad-57 device as the Rad-57 recordings were not taken in direct sunlight or in proximity to strobing light, and it is not standard practice to use them, although recommended by the manufacturer. The Nonin device requires no light shield.

Conclusions

These results suggest the new Nonin CO-Met™ Noninvasive Oximetry System delivers reliability in a fire rehabilitation environment and a reading in keeping with expected outcomes.

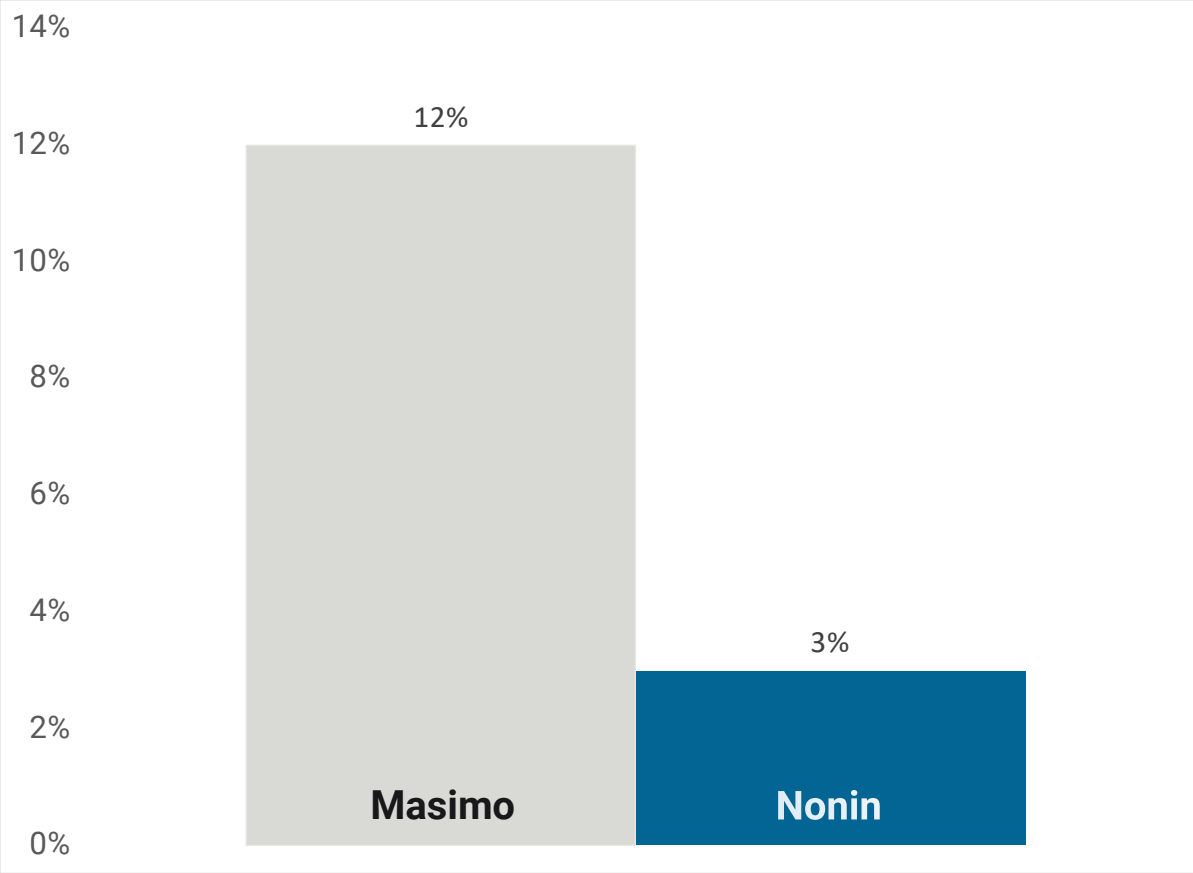
[1]HealthEast Medical Transport, St. Paul, MN, USA

Presented at the 2018 European Society for Emergency Medicine Congress (EUSEM)

Glasgow, Scotland

The chart below shows the percentage of COHb readings that did not display for each device.

COHb Readings That Did Not Display



Known smoker readings comparing the Nonin and Masimo devices.

Subject	Nonin COHb	Masimo SpCO
#35 Reading 1	8	1
#35 Reading 2	12	No Reading

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