4. Touger M, Birnbaum A, Wang J, Chou K, Pearson D, Bijur P. Performance of the RAD-57 pulse co-oximeter compared with standard laboratory carboxyhemoglobin measurement. Ann Emerg Med 2010;56(4):382-388.
5. Roth D, Herkner H Schreiber W, Hubmann N, Gamper G, Laggner AN, Havel C. Accuracy of noninvasive multiwave pulse oximetry compared with carboxyhemoglobin from blood gas analysis in unselected emergency department patients. Ann Emerg Med 2011;58(1):74-79.
6. Mahoney JJ, Vreman HJ, Stevenson DK, Van Kessel AL. Measurement of carboxyhemoglobin and total hemoglobin by five specialized spectrophotometers (CO-oximeters) in comparison with reference methods. Clin Chem 1993;39(8):1693-1700.
7. Masimo Corporation. RAD-57 operator's manual. Masimo Rainbow SET signal extraction pulse CO-oximeter. 2006.
8. Severinghaus JW, Kelleher JF. Recent developments in pulse oximetry. Anesthesiology 1992;76(6):1018-1038.
9. Bledsoe B, McEvoy M. Where there's CO; there's not always fire: how pulse CO-oximetry serves as an important assessment and triage tool. JEMS 2009;34:5-8.
10. Stankovic AK, Smith S. Elevated serum potassium values: the role of preanalytic values. Am J Clin Pathol 2004;121(Suppl 1):S105-S112.

DOI: 10.4187/respcare.02737

S_{pCO}: Let's Not Throw the Baby Out With the Bath Water—Reply

In reply:

We thank Dr McEvoy for his thoughtful reply to our report. He is correct that our definition of false positive was restrictive; however, we based this definition on the manufacturer's stated accuracy specification, and, indeed, found that the RAD-57 functioned as specified. When broadened to include 2 standard deviations (95% of the data), the accuracy range would be ± 6%, a range that is challenging for the purpose of diagnosing CO poisoning.

We readily acknowledge that technician technique may play a role in obtaining accurate data, even though our technicians and study team were trained by the manufacturer on probe placement. Our concern is that, whether by technical limitations or operator error, the RAD-57 may provide an erroneously low S_{pCO} measurement in a patient with CO poisoning. We agree that S_{pCO} technology can be valuable in broadly screening for occult CO poisoning. We offer that an elevated S_{pCO} should raise concern about CO poisoning, especially if the evaluating clinician has not considered CO exposure. However, we strongly caution against using S_{pCO} measurement to rule out CO poisoning when symptoms and circumstances suggest it. Returning a misdiagnosed patient to the scene of the poisoning can have devastating and even deadly consequences.

Lindell K Weaver MD
Susan K Churchill APRN-NP
Kayla Deru
Hyperbaric Medicine
LDS Hospital
Salt Lake City, Utah

The authors have disclosed relationships with SciMetrika and Masimo.

DOI: 10.4187/respcare.02760

S_{pCO}: Let's Not Throw the Baby Out With the Bath Water—Reply

In reply:

The study by Weaver and colleagues[1] demonstrated that, while the RAD-57 CO-oximeter operated within the manufacturer's specifications, with 68% of S_{pCO} measurements falling within ± 3% of the laboratory carboxyhemoglobin (COHb) measurements of < 40%, in several cases the S_{pCO} reported by the RAD-57 underestimated the COHb. This raises concerns about the utility of the RAD-57 in identifying cases of occult CO poisoning, which is one of the primary potential benefits of a point-of-care noninvasive carboxyhemoglobin screening test. Furthermore, Weaver et al's findings were consistent with other studies of the RAD-57.[2-4]

In response to Weaver et al's study, Dr McEvoy opines that these failures of the RAD-57 to report a S_{pCO} consistent with the laboratory COHb measurement could have been due to technician technique. The concern has previously been raised by another industry representative,[5] in response to a prospective study that demonstrated wide limits of agreement and poor sensitivity of the RAD-57.[2] While technique may have been a contributor to the discrepancy between S_{pCO} and COHb in Weaver et al's study, this does not excuse the failure of the RAD-57 to identify elevated COHb levels. The use of any medical device is not isolated from user technique or user error, and dismissing false negative results described by Weaver et al and others as being due to poor technique ignores the potential consequences of broadening the clinical use of the RAD-57. If false negative values were obtained under relatively idealized settings (technicians were trained by industry representatives and were obtaining measurements in the setting of a research study), it is reasonable to assume that the rate of false negatives will not be lower in the non-idealized setting of real world clinical medicine, where attention to technique may be less meticulous than in a research study.

Given these considerations, the poor sensitivity, rate of false negatives, and the inaccuracy of the RAD-57 should be a warning to medical personnel that S_{pCO} is not definitive, and that a normal S_{pCO} should not be reassuring. Ultimately, the false negatives obtained by the RAD-57, whether due to technician technique, intrinsic device inaccuracies, or patient-level factors, demonstrates that the RAD-57 is not suitable as a screening device and that there is potential for measurement inaccuracies and patient harm in real world clinical settings.

We agree that further work to develop an accurate, precise, user-friendly, and non-invasive S_{pCO} monitor is warranted, and that a rapid, accurate, point-of-care carbon monoxide monitor would be extremely valuable. The RAD-57 monitor, however, does not meet these criteria, based on the available clinical data, and there is insufficient evidence for its broad clinical use.[1-4]

Jeremy B Richards MD MA
Pulmonary, Critical Care, and Sleep Medicine
Beth Israel Deaconess Medical Center
Boston, Massachusetts

Susan R Wilcox MD
Department of Anesthesia and Critical Care
Massachusetts General Hospital
Boston, Massachusetts

The authors have disclosed no conflicts of interest.

REFERENCES

1. Weaver LK, Churchill SK, Deru K, Cooney D. False positive rate of carbon monoxide

saturation by oximetry of emergency department patients. Respir Care 2013;57(2): 232-240.
2. Touger M, Birnbaum A, Wang J, Chou K, Pearson D, Bijur P. Performance of the RAD-57 pulse CO-oximeter compared with standard laboratory carboxyhemoglobin measurement. Ann Emerg Med 2010;56(4): 382-388.
3. Ruppel GL, Wilson HA, Gall VK, Hempkens JA. Multi-wavelength pulse oximeter is not suitable for adjusting D_{LCO} measurements. Respir Care 2011;56(8):1115-1121.
4. O'Malley GF. Non-invasive carbon monoxide measurement is not accurate. Ann Emerg Med 2006;48(4):477-478.
5. O'Reilly M. Performance of the RAD-57 pulse co-oximeter compared with standard laboratory carboxyhemoglobin measurement. Ann Emerg Med 2010;56(4):442-444.

DOI: 10.4187/respcare.02769

Anxiety Disorders in Patients With COPD

To the editor:

We read the interesting review by Willgoss and Yohannes "Anxiety Disorders in Patients With COPD: A Systemic Review."[1] Willgoss et al found similarly high levels of anxiety in both in-patient and out-patient samples, and suggested that such a high incidence cannot be explained solely by the presence of an exacerbation-related hospitalization. Rather, anxiety in patients with COPD is most likely to be a chronic and disease-related phenomenon.[1] Their findings also revealed the high prevalence of specific anxiety disorders, including panic disorder and phobic anxiety disorders, with panic disorder being particularly common in patients with COPD.[1]

However, one of the common, yet underdiagnosed, comorbidities that complicates the clinical picture of patients with COPD is the overlap syndrome: the coexistence of obstructive sleep apnea (OSA) and COPD.[2,3] Lacedonia et al studied 720 patients with suspected OSA, of whom 168 had overlap syndrome, and 86 had COPD.[4] They found that the overlap syndrome group had lower daytime P_{aO_2} than the OSA group, and the diurnal P_{aO_2} in the overlap syndrome group correlated with age and with FEV_1.[4] Overlap syndrome causes more severe nocturnal hypoxemia than either OSA or COPD alone.[2,4] Therefore, overlap syndrome contributes to daytime hypoxemia and the embarrassing breathlessness, resulting in worsening anxiety and social phobia.

Furthermore, patients with overlap syndrome experience nocturnal hypoxemia, especially during rapid eye movement sleep,[2] resulting in nighttime awakening, which may be associated with "sensation of suffocation or choking" and fear of death. Those episodes may carry nighttime anxiety to daytime, making anxiety a 24 hour ongoing disorder.

Clinical screening for overlap syndrome should be part of the evaluation of anxiety in patients with COPD, and that should be followed by polysomnography if warranted.[3] Appropriate therapy for overlap syndrome, which may include CPAP and nocturnal oxygen, should be applied. Lack of this therapy may make other treatment modalities, such as antidepressants and psychotherapy, not as effective in reducing anxiety, panic attacks, and number of hospital admissions in patients with COPD.

Samer Alkhuja MD
Pocono Medical Center
The Commonwealth Medical College
East Stroudsburg, Pennsylvania

The author has disclosed no conflicts of interest.

REFERENCES

1. Willgoss TG, Yohannes AM. Anxiety disorders in patients with COPD: a systemic review. Respir Care 2013;58(5):858-866.
2. Owens RL, Malhotra A. Sleep-disordered breathing and COPD: the overlap syndrome. Respir Care 2010;55(10):1333-1344.
3. López-Acevedo MN, Torres-Palacios A, Elena Ocasio-Tascón M, Campos-Santiago Z, Rodriguez-Cintrón W. Overlap syndrome: an indication for sleep studies? A pilot study. Sleep Breath 2009;13(4):409-413.
4. Lacedonia D, Carpagnano GE, Aliani M, Sabato R, Foschino Barbaro MP, et al. Daytime P_{aO_2} in OSAS, COPD and the combination of the two (overlap syndrome). Respir Med 2013;107(2):310-316.

DOI: 10.4187/respcare.02716

Anxiety Disorders in Patients With COPD—Reply

In reply:

We are most grateful for Dr Alkhuja's intriguing comments on our review published in RESPIRATORY CARE.[1] He raised 2 important, inter-related questions. First, Dr Alkhuja highlights the importance of under-diagnosed comorbidities and their consequences in patients with COPD. In this context, comorbid obstructive sleep apnea (OSA) in patients with COPD, which is often described as the overlap syndrome, is under-recognized and inadequately managed in COPD patients. A recent elegant study by Mann and co-workers[2] found that untreated overlap syndrome in COPD patients was associated with elevated risk of death and hospitalization due to exacerbation, compared to patients who used CPAP. Furthermore, the overlap of COPD with OSA may increase the susceptibility to arterial stiffness, which in turn predisposes to pulmonary hypertension[3] and decline in cognitive function.

Second, the association of overlap syndrome with comorbid anxiety has not been fully investigated. This is partly due to the over-lapping clinical symptoms of COPD that may mask the symptoms of OSA. This requires specialized training in sleep medicine for the healthcare professionals (eg, primary care physicians and advanced practice nurses) and comprehensive assessment to detect OSA in COPD patients.

The focus of our systematic review was primarily to underscore the prevalence and the existence of a wide range of clinical anxiety disorders in patients with COPD, which are often not fully recognized and treated. Therefore, we have not explored the association between overlap syndrome and/or OSA in patients with COPD. However, we concur with Alkhuja that OSA is a disabling comorbid disease that may be a risk factor for anxiety.[4] The co-occurrence of OSA in COPD patients increases the frequency of oxygen desaturation,[4] defragments the quality or quantity of sleep due to hypoxemia and hypercapnia, and results in depression, somnolence, and daytime dreaming.[5] All these factors contribute to COPD patients' increasing burden and worsening prognosis of anxiety symptoms and dependence on their caregivers. Hence, regular screening and monitoring for OSA and anxiety symptoms in patients with COPD is worthy of consideration. Indeed, it will be the first step to detect these disorders and refer patients to sleep centers to receive appropriate treatment.

Finally, there is a lack of robust data on the impact of overlap syndrome and the potential mechanism and its association with cardiovascular disease and COPD. Thus, further studies are required to examine the role of hypoxemia, systemic inflammation, OSA, and clinical anxiety in patients with COPD.