Development and Testing of Formal Protocols for Oxygen Prescribing

GORDON H. GUYATT, DOUGLAS A. McKIM, BRUCE WEAVER, PEGGY A. AUSTIN, ROBERT E. J. BRYAN, STEPHEN D. WALTER, MIKA L. NONOYAMA, IVONNE M. FERREIRA, and ROGER S. GOLDSTEIN

Department of Clinical Epidemiology and Biostatistics and Department of Medicine, McMaster University, Hamilton, Ontario, Canada; Department of Medicine, University of Ottawa, Ottawa, Ontario, Canada; Department of Respiratory Medicine, West Park Hospital, Toronto, Ontario, Canada; and Department of Medicine, University of Toronto, Toronto, Ontario, Canada

The absence of standardized assessment protocols with well-defined measurement properties limits comparison of outcomes among those receiving long-term oxygen therapy (LTOT). We describe simple protocols for a hospital test, a simulated home test, and an actual home test, their reliability and relationship to each other. Stable patients with exercise hypoxemia participated. In 74 patients who completed four exercise tests, correlations between tests ranged from 0.85 to 0.78. Of these 27.0% had the same prescription from all four tests. In 46% prescriptions were within 1 L/min and in 27% within 2 L/min. During exercise the hospital tests suggested slightly higher oxygen prescriptions than did the simulated home tests (2.5 L/min versus 2.0 L/min, $p < 0.001$). In 23 patients who participated in actual home assessments, the correlations between the home test, the hospital, and the simulated home tests were 0.22 (95% CI −0.24 to 0.67) and 0.27 (95% CI −0.18 to 0.72). In conclusion, standardizing tests for the assessment of LTOT is important. We describe simple hospital and simulated home tests that are reproducible, easy to carry out, and correlate well with each other.

Two randomized trials have demonstrated that long-term oxygen therapy (LTOT) can prolong the lives of patients with hypoxemic chronic obstructive lung disease (1, 2). Patients who meet the inclusion criteria for these studies almost certainly benefit from supplemental oxygen, whereas the benefit for those who do not remains unclear.

In those who meet criteria, clinicians must decide on the optimal prescription of oxygen. Neither of the previously published randomized trials provided a detailed protocol as to how the oxygen dose was determined. In the nocturnal oxygen therapy trial (NOTT) patients received the lowest flow of oxygen that increased their semirecumbent arterial P_{O_2} by at least 6 mm Hg and maintained their resting $P_{O_2} > 60$ mm Hg with 1 L/min more during sleep and exercise. In the British MRC trial patients received 2 L/min, or a higher flow if necessary, to achieve a resting $P_{O_2} > 60$ mm Hg. The investigators provided no information on oxygen flow during exercise or sleep.

Many clinicians regard an optimal oxygen prescription as the minimal flow that achieves an adequate saturation during all normal activities. Although the definition of "adequate" varies, the flow of oxygen required to maintain the saturation above 90% at rest as well as during daily activities is a commonly used threshold. Once the resting oxygen prescription has been established exercise desaturation will often occur during daily activities (3). Therefore clinicians frequently prescribe a higher flow during exercise.

(*Received in original form February 28, 2000 and in revised form October 3, 2000*)

Correspondence and requests for reprints should be addressed to Roger S. Goldstein, West Park Hospital, 82 Buttonwood Ave., Toronto, ON, M6M 2J5 Canada. E-mail: rgoldste@westpark.org

Am J Respir Crit Care Med Vol 163. pp 942–946, 2001
Internet address: www.atsjournals.org

Oxygen prescription protocols vary. Not only does the absence of a standard approach make it difficult to compare patient outcomes, adopting any particular approach is limited by not having a clear idea of the measurement properties of the various protocols.

Although some patients are prescribed LTOT using a hospital assessment, in others testing occurs outside of the hospital environment. A standardized, reproducible assessment of a patient's oxygen prescription that could be carried out at home or at a health care facility would facilitate efficient health-care delivery. However, space limitations at home often preclude the type of assessment that can be carried out in the hospital setting, especially during exercise.

We have therefore developed protocols for hospital or home-based assessments of hypoxemia that could be used to prescribe LTOT. By suggesting detailed explicit criteria for each decision point in the protocol, we hoped to maximize the reproducibility and validity of the measures. Because of the logistical challenges of testing patients in their homes we developed a simulated in-home test conducted in the hospital. In this study we describe our testing protocols, addressing issues of reliability for both the hospital and the simulated home tests as well as their relation to one another and to testing conducted in the home.

METHODS

Recruitment

We enrolled two groups of patients. The first group of patients participated in respiratory rehabilitation programs in Toronto or Ottawa. The second group of patients had been assessed in their homes for the appropriateness of domiciliary oxygen, which was prescribed by their physicians and provided by a government-funded home oxygen program (HOP). Both groups of patients met the following criteria: (*i*) a primary diagnosis of chronic obstructive pulmonary disease (COPD); (*ii*) clinically stable at the time of each test; (*iii*) previous or current prescription of oxygen at rest or during exercise or current oximetry suggesting desaturation at rest or during exercises (oxygen saturation < 88% on at least one occasion); (*iv*) highest measured $FEV_1 < 70\%$ predicted; and (*v*) highest measured $FEV_1/FVC < 70\%$ predicted. We excluded patients who had conditions other than COPD, in particular cardiovascular disease or arthritis, that might limit their ability to exercise.

Protocols

We conducted all testing between May 7, 1998 and Noveber 27, 1998.

Resting Oxygen Prescription

Patients breathing room air were asked to sit upright. Before beginning any test, the respiratory therapist (RT) would check that the pulse oximeter identified itself as having an acceptable signal and that the oximeter bar was pulsing to show the heart rate or the waveform was in synchrony with the heart rate. The RT checked the patient's pulse to ensure that it corresponded to the oximeter signal. Fingernail polish, if worn by the patient, was removed before testing.

Patients' oxygen saturation was checked by finger or ear oximetry for 20 min (Nellcor N-20, probe Durasensor DS-100A), or until satu-

ration (Sp_{O_2}) fell below 80%. If the Sp_{O_2} was below 90% the RT administered oxygen by nasal cannulas at 1 or 2 (if Sp_{O_2} was $< 85\%$) L increments to achieve an Sp_{O_2} of $\geq 90\%$. The RT increased the oxygen flow at 20-min intervals to ensure that each measured Sp_{O_2} was under stable conditions.

Exercise Oxygen Prescription: Hospital Test

The tests were conducted in the morning, at approximately 10:00 A.M. The patients used their bronchodilators according to their usual schedule, typically around 7:30 A.M. Time of day for testing was consistent for every patient. The RT requested that the patient walk for 5 min at a pace that "you find comfortable and would use to walk on a day to day basis" and to "breathe naturally" during the test. The resting oxygen flow was administered. The patient walked in a corridor 30 m in length for 5 min. The RT carried the oxygen and oximeter, either using a cart or manually. If patients ordinarily used a cane, walker, or rollater, they used the aid during the test. The RT recorded heart rate and saturation, both from the pulse oximeter, throughout the test. If the patient desaturated to $< 90\%$ for $> 20\%$ of the duration of the test it was repeated. If the Sp_{O_2} was in the range of 80% to 84% the flow was increased by 2 L/min, if the range was 85% to 89% the flow was increased by 1 L/min. Patients rested for 20 min between tests. Oxygen flow was considered adequate if the Sp_{O_2} was $\geq 90\%$ for $\geq 80\%$ of the test.

Exercise Oxygen Prescription: Home Tests

The patient was asked to walk for 15 s at a comfortable pace between two points and then walk on the spot at the same pace for 15 s. For the test performed in the patient's home ("home test"), they were as far apart as the patient's living situation permitted. For the "simulated home test" that was performed in the hospital, the two points were 5 m apart. If patients ordinarily used a cane, walker, or rollater, they used the aid during the test. The patients used their own oxygen delivery. A tape recording counted the last 3 s of each 15-s interval and then instructed the patient to "now walk on the spot" or "now walk." Each test was 5 min in duration. The RT recorded heart rate and saturation throughout the test. The criteria for altering oxygen flow, or for considering the flow adequate, were identical to the in-hospital test.

Reliability Testing

There were three protocols for exercise as described above. Two were conducted in the hospital (the "hospital test" and the "simulated home test"). Some patients agreed to carry out the test in their home ("home test"). We asked patients to attend for 2 d at the hospital. During each day they completed one "hospital test" and one "simulated home test." We constructed a randomization schedule that balanced two test orders: home/hospital/home/hospital and hospital/home/hospital/home. We recognized that some patients who had completed an assessment in their homes might specify in advance that they would be willing to undertake only two tests (i.e., willing to visit the hospital only once). Therefore, we also constructed a separate randomization schedule for this possibility. Seventeen assistants (respiratory therapists) participated in the testing. No RT conducted more than one rest test with the same patient and in only one case did the same RT conduct more than one exercise test on the same patient. The RTs were blinded to the results of all tests conducted by other RTs. Patients completed their hospital tests within a period of 2 wk.

Statistical Analysis

We began by conducting a repeated measures analysis of variance (ANOVA) with oxygen prescriptions at rest as the dependent variable. In this analysis we included patients who had completed four tests (two hospital and two simulated home tests). The independent variables were hospital versus simulated home testing, the two test orders, first or second testing session, and all of the interaction terms. The interaction terms address whether status on one variable influences the effect of another variable. For instance, it could be possible that the amount of oxygen required might be greater for the hospital than the simulated home test during the first testing session, but not the second. We then conducted an analysis including patients who had completed four exercise tests. The result of the exercise test (that is, the oxygen flow required to achieve normoxemia) was the dependent variable and the independent variables were the same as for the rest test.

We then conducted analyses including all patients who had completed a true home test, a hospital test, and a simulated home test. For these analyses, the independent variables were type of test (home, hospital, simulated home), test order (home/hospital/simulated home versus home/simulated home/hospital), and the two-way interaction. The dependent variable in one analysis was the oxygen flow required to achieve rest normoxemia, and in the other the oxygen flow required to achieve exercise normoxemia.

For all of the analyses described above, we calculated all pair-wise Pearson correlations and weighted kappas between the three or four oxygen prescriptions. Because the results of the Pearson correlations and the weighted kappas were very similar, we report only the former. We also used methods described by Steiger (4) and software available at http://www.interchg.ubc.ca/steiger/multi.htm to test for differences in each of the four correlation matrices. In all analyses, because of the multiple tests undertaken, we interpreted a p value of 0.01 or less as significant.

We calculated the proportion of patients in whom the four rest tests yielded no differences in prescription, and differences of 1, 2, 3, and 4 L. We made the same calculations for the four exercise tests. We calculated the mean of the four rest tests and the mean of the four exercise tests and the differences between these means that we rounded to the nearest whole number.

TABLE 1. CHARACTERISTICS OF THE 88 PARTICIPATING PATIENTS

Mean age in years (SD)	67.5 (8.4)
Number of females	42 (47.7%)
Smoking status	
Never smoked	6 (6.8%)
Current smokers	2 (2.3%)
Ex-smokers	80 (90.9%)
Pack-years smoked (SD)	43.4 (22.1)
Medication	
Inhaled β-agonists	83 (94.3%)
Inhaled ipratropium bromide	73 (83.0%)
Inhaled steroid	62 (70.5%)
Forced expired volume in 1 s	
Absolute (SD)	0.7 (0.4)
Percent predicted (SD)	31.8 (15.8)
Forced vital capacity	
Absolute (SD)	1.8 (0.7)
Percent predicted (SD)	56.4 (19.2)
Six-minute-walk test distance in meters (SD)	303.3 (86.5)

RESULTS

We identified 100 eligible patients of whom 93 agreed to participate. Table 1 presents the characteristics of 88 patients who completed at least one of four in-hospital rest tests, four in-hospital exercise tests, or one true home test and at least one hospital and one simulated home test. Table 2 depicts the tests that the patients undertook. Of the patients, 78 completed

TABLE 2. TESTS COMPLETED BY PARTICIPATING PATIENTS

	65 Rehabilitation Patients	23 Home Oxygen Patients
Rest measurements		
Four rest measures in hospital	65 patients	13 patients*
Two rest measures in hospital, one in the home		10 patients
Exercise measurements		
Four exercise measures in hospital	61 patients	13 patients*
Two exercise measureas in hospital, one at home		9 patients

* These patients also had rest and exercise tests in the home.

TABLE 3. CORRELATION MATRIX (PEARSON'S r) FOR THE FOUR REPETITIONS OF THE REST OXYGEN REQUIREMENT ASSESSMENT CONDUCTED IN THE HOSPITAL IN 82 PATIENTS

	First Hospital	Second Hospital	First Simulated Home	Second Simulated Home
First hospital		0.73	0.77	0.74
Second hospital			0.66	0.77
First simulated home				0.79

four rest tests and 74 completed four exercise tests. For rest and exercise tests, respectively, 23 and 22 patients completed the prior home test and at least one hospital and one simulated home test. The median duration of time between the home assessment and the in-hospital assessment was 106 d, with a range from 2 to 208 d and an interquartile range from 51 to 153. Of the 78 patients who attended for two in-hospital assessments, all had their tests within 14 d of one another.

Rest Test Results

In the 78 patients who had four resting assessments conducted in hospital, the number of patients with each rest prescription was very similar across the four repetitions. Between 54 and 57 (69.2% to 73.1%) required no oxygen at rest, between 15 and 18 (19.2% and 23.1%) required 1 L/min, between 2 and 6 (2.6% to 7.7%) required 2 L/min, and 2 (2.6%) required 3 or more L/min. The mean and standard deviation of oxygen dose for the four hospital tests were 0.4 and 0.7 L/min, respectively, for three of the four repetitions and 0.5 and 0.9 L/min for the fourth. In the repeated measures analysis of variance we found no effects of type of test, test session, order of testing, or any interactions.

Table 3 presents a correlation matrix for the four repetitions of the test. All correlations are moderate to high, and are very similar to one another. The null hypothesis of no differences among the pairwise correlations could not be rejected using Steiger's test (4), $p = 0.11$. The similarity in results is not surprising as the four tests were conducted with identical protocols. The 95% confidence interval around the highest correlation, 0.79, was 0.66 to 0.93. The 95% confidence interval around the lowest correlation, 0.66, was 0.48 to 0.83.

Of the 78 patients, 49 (62.8%) had the same rest prescription from all four tests, 24 (30.8%) had all four prescriptions within 1 L of one another, 4 (5.1%) had all four prescriptions within 2 L, and 1 (1.3%) received prescriptions that varied by as much as 4 L/min.

In the 23 patients with true home rest assessments the number (and thus the percentages) of patients with each rest prescription was similar across the three repetitions. Between 9 and 13 (39.1% to 56.5%) required no oxygen at rest, between 6 and 9 (26.1% and 39.1%) required 1 L/min, between 2 and 4 (8.7% to 17.4%) required 2 L/min, and between 1 and 3 (4.3% and 13.0%) required 3 or more L/min. In the repeated measures analysis of variance we found no effects of type of test. The correlation between the hospital and simulated home test was 0.48 (95% confidence interval 0.08 to 0.88), and correlations between the home test and the hospital and simulated home tests were 0.57 (95% CI 0.19 to 0.94) and 0.79 (95% CI 0.51 to 1.0).

TABLE 4. EXERCISE PRESCRIPTIONS FROM FOUR EXERCISE TESTS CONDUCTED IN THE HOSPITAL IN 74 PATIENTS

Prescription	First Simulated Home Test	Second Simulated Home Test	First Hospital Test	Second Hospital Test
No oxygen	7 (9.5%)	7 (9.5%)	6 (8.1%)	6 (8.1%)
1 L/min	26 (35.1%)	21 (28.4%)	15 (20.3%)	17 (23.0%)
2 L/min	18 (24.3%)	23 (31.1%)	15 (20.3%)	13 (17.6%)
3 L/min	14 (18.9%)	13 (17.6%)	22 (29.7%	21 (28.4%)
4 L/min	4 (5.4%)	3 (4.1%)	7 (9.5%)	8 (10.8%)
5 L/min	4 (5.4%)	6 (8.1%)	9 (12.2%)	5 (6.8%)
6 L/min	1 (1.4%)	1 (1.4%)	0	4 (5.4%)
Mean (SD)	2.0 (1.4)	2.1 (1.4)	2.5 (1.5)	2.5 (1.6)

Exercise Test Results

Table 4 presents the results of the exercise prescription assessment for the 74 patients who had all four exercise tests and demonstrates similar distributions of oxygen requirements using the two simulated in-home tests and the two hospital tests. However, the two hospital tests tended to result in higher oxygen prescriptions than the two simulated home tests. This is reflected in the mean values: first simulated home 2.0 (standard deviation 1.4), second simulated home 2.1 (1.4), first hospital 2.5 (1.5), and second in 2.5 (1.6). The analysis of variance showed that the difference between home and hospital tests was highly significant ($p < 0.001$). The only other significant effect in the analysis was an interaction between hospital versus simulated in-home test and the order of testing. When the simulated in-home test was conducted first, the mean values for simulated in-home and in-hospital tests were 2.0 and 2.7. When the patients completed the hospital test first the mean value for the simulated home test was 2.1 and the hospital test 2.3. Thus, the difference between the simulated home and the hospital test was larger when the home test was conducted first than when the hospital test was conducted first.

Despite the systematic differences in exercise oxygen requirements—larger flow prescriptions with the hospital test—the correlations between replicate tests, and across simulated home and hospital tests, was higher for the exercise than for the rest tests (Table 5). Further, the correlations between simulated home and hospital tests was very similar to the correlation between the two simulated home tests, and between the two hospital tests. The 95% confidence interval around the highest correlation, 0.85, was 0.73 to 0.98. The 95% confidence interval around the lowest correlation, 0.78, was 0.63 to 0.92. Steiger's test for differences among the six elements of the correlation matrix was not significant ($p = 0.34$).

Of the 74 patients who completed four exercise tests, 20 (27.0%) had the same exercise prescription from all four tests, 34 (45.9%) had all four prescriptions within 1 L of one another, 14 (18.9%) had all four prescriptions within 2 L, 4 (5.4%) received prescriptions that varied by as much as 3 L/min, and 2 (2.7%) by as much as 4 L.

In the 22 patients who completed the actual home exercise test, results differed substantially between the home and hospital tests (Table 6). Although the ANOVA failed to show any significant main effects or interactions, tests done in the hospital suggested higher exercise oxygen requirements than

TABLE 5. CORRELATION MATRIX (PEARSON'S r) FOR THE FOUR REPETITIONS OF THE EXERCISE OXYGEN REQUIREMENT ASSESSMENT CONDUCTED IN THE HOSPITAL IN 77 PATIENTS

	First Hospital	Second Hospital	First Simulated Home	Second Simulated Home
First hospital		0.82	0.79	0.79
Second hospital			0.78	0.85
First simulated home				0.82

TABLE 6. EXERCISE PRESCRIPTIONS IN 22 PATIENTS WITH TRUE HOME ASSESSMENTS OF OXYGEN REQUIREMENTS

Prescription	True Home Test	Simulated Home Test	Hospital Test
No oxygen	1 (4.5%)	0	1 (4.5%)
1 L/min	3 (13.6%)	3 (13.6%)	1 (4.5%)
2 L/min	10 (45.5%)	7 (31.8%)	5 (22.7%)
3 L/min	4 (18.2%)	7 (31.8%)	6 (27.3%)
4 L/min	1 (4.5%)	1 (4.5%)	7 (31.8%)
5 L/min	3 (13.6%)	4 (18.2%)	2 (9.1%)
Mean (SD)	2.5 (1.3)	2.8 (1.3)	3.1 (1.3)

those done in the home (Table 6). The mean value and standard deviation for the home test were 2.5 (1.3), for the simulated home test 2.8 (1.3), and for the hospital test 3.1 (1.3). The correlation between the hospital and simulated home test was 0.45 (95% CI 0.03 to 0.86), whereas the correlations between the actual home test and the hospital and the simulated home tests were, respectively, 0.22 (95% CI −0.24 to 0.67) and 0.27 (95% CI −0.18 to 0.72). Steiger's test revealed no significant differences among these correlations ($p = 0.62$).

Difference between Rest and Exercise Test Results

None of the differences in mean rest and exercise prescriptions showed greater oxygen flow at rest. Of the 74 patients who had four rest and four exercise assessments, 4 (5.4%) had no differences in rest and exercise prescription, 24 (32.4%) had 1 L more on exercise, 22 (29.7%) had 2 L more on exercise, 17 (23.0%) had 3 L more on exercise, 5 (6.8%) had 4 L or more on exercise, 1 (1.4%) had 5 L more on exercise, and 1 (1.4%) had 6 L or more on exercise.

We found that 29.1% of our patients would receive the same exercise prescription (1 L/min more than the rest prescription) with the NOTT approach compared with an individual assessment. Another 4.7% would receive 1 L less than the NOTT approach (that is, the same as the rest prescription), whereas 31.4% would receive 1 L more than the NOTT approach (that is, 2 L more than their rest prescription). The remaining 34.8% would receive 2 or more L/min more than the NOTT approach.

DISCUSSION

In this study we developed protocols for the home or hospital assessment of oxygen requirements and tested their reproducibility. Over a period of 2 wk both the rest tests (Table 2) and the exercise tests (Table 4) showed high correlations with one another. The simulated home tests bore as strong a correlation with the hospital tests as the hospital tests did with one another. However, the hospital prescription was, on average, 0.5 L/min more than the home prescription.

Given the lower oxygen prescriptions of the simulated home test, it is not self-evident which prescription is superior. This will depend on which level of exertion most closely simulates what patients actually undertake. Placing a high value on avoiding exercise hypoxemia would suggest the superiority of the hospital test. A priority on avoiding unnecessary resource consumption would favor use of the simulated home results.

Another way of looking at agreement is the extent to which all four tests yielded the same or similar prescriptions. For the four rest tests 62.8% yielded the same prescription and in 93.6% the four prescriptions were within 1 L of each other. Despite the higher correlation, the uniformity of prescription was not as great in the exercise prescriptions: 27.0% had the same prescription from all four tests and 73.0% had all four prescriptions within 1 L of one another. The greater variability in exercise prescription results explains the discordance between the correlations and the raw agreement.

Agreement between the actual home exercise test and the simulated home and hospital tests was much poorer. One explanation for the difference in results between the actual home and the simulated home tests is chance—plausible, because we tested only 22 patients at home. Another is that testing among the at-home patients was less reproducible than testing among the rehabilitation patients who might be more familiar with exercise tests as their program included regular exercise. The lower correlations with respect to resting and exercise oxygen between the in-hospital tests in these patients suggest this possibility. A third possibility relates to the time between tests. The in-hospital tests were all conducted within a period of 2 wk. The median time between the home and hospital assessments was greater than 3 mo—a time long enough for clinical changes to have occurred, notwithstanding our efforts to ensure that we were testing a clinically stable population. If the last explanation is correct, it suggests the need for repeated testing over shorter periods of time to optimize exercise oxygen prescription.

In the NOTT trial all patients received an exercise prescription that was 1 L/min greater than their rest prescription. To what extent do individual exercise oxygen assessments yield different prescriptions? We found that 29.1% of our patients would receive the same exercise prescription (1 L/min more than the rest prescription), with the NOTT approach compared with an individual assessment. Almost all the others would receive more oxygen with an individualized approach: approximately one-third would receive 1 L more, and another one-third would receive 2 or more L/min more than the NOTT approach. These discrepancies define the boundaries of possible additional benefit that clinicians might achieve by individually titrating the exercise oxygen prescription, and the likely additional cost involved in the titration and subsequent oxygen administration.

Continuous oxygen saturation monitoring in the home represents another method of assessing the possible need for domiciliary oxygen. Results of continuous monitoring in patients receiving home oxygen, or those with reduced resting P_{O_2} above 55 mm Hg, are consistent with our data in showing that desaturation with exercise is commonplace (5–9). Investigators have not, however, assessed the day-to-day or week-to-week reproducibility of home monitoring.

We see the essential messages of our study as follows. First, rigorously developed protocols for the determination of levels of oxygen required to prevent exercise hypoxemia achieve moderate levels of reproducibility when administered in the hospital setting. It is likely that unstandardized testing is much more variable. Second, achieving reproducible results in the home appears much more difficult. Third, standardized testing leads, in most patients, to exercise prescriptions of 1 to 2 L more than clinicians would prescribe if they followed the NOTT protocol.

Our results suggest a number of steps toward achieving better oxygen prescription protocols. First, other investigators should test our protocol (or modifications that they prefer) to ensure that our results are reproducible. This work should lead to widely accepted standardized protocols for determining levels of oxygen administration necessary to relieve hypoxemia in day-to-day exercise. Second, investigators should endeavor to develop protocols that can be reproducibly administered in the home.

Our study examined protocols for minimizing hypoxemia associated with exercise. We did not address the impact that minimizing hypoxemia might have on patient-important out-

comes such as improving quality of life through reducing dyspnea during day-to-day activities, reducing hospitalizations, or prolonging life. Evidence of benefit of oxygen for patients with exercise, but not rest, hypoxemia, comes predominantly from measures of dyspnea during laboratory exercise (10–12). The strongest study to date, a randomized double-blind trial of oxygen in the home, failed to show any benefit of treating transient exercise hypoxemia on activities of daily living (13). Furthermore, no trials have demonstrated a decrease in morbidity or mortality through relief of exercise hypoxemia. Therefore, once the respiratory community has agreed on protocols for determining exercise oxygen prescriptions to prevent desaturation in day-to-day activities, investigators should conduct further studies to determine which, if any, patients with significant exercise but not resting hypoxemia benefit from domiciliary oxygen. Development of well-defined protocols for prescribing oxygen is a critical first step that will permit rigorous assessment of patient-important outcomes of oxygen therapy.

***Acknowledgment*:** The authors would like to express our gratitude to the following respiratory therapists who conducted the testing: Susan Toth, Zehra Ali, Carman Osbourne, Sandra Persaud, Bruce Kripp, Shilpa Pathare, Joan Norgren, Laurie Taylor, Marty Penner, Donna Trotti, Jason Pearce, Natalie Martin, Melanie Lasage, Julie McMahon, Derry Thibeault, and June Meager.

References

1. Report of the Medical Research Council Working Party. Long term domiciliary oxygen therapy in chronic hypoxic cor pulmonale complicating chronic bronchitis and emphysema. *Lancet* 1981;1:681–686.
2. Kvale PA, Cuggell DW, Anthonisen NR, Timms RM, Petty TL, Boylen CT, Nocturnal Oxygen Therapy Trial Group. Continuous or nocturnal oxygen therapy in hypoxemic chronic obstructive lung disease. *Ann Intern Med* 1980;93:391–398.
3. Sliwinski P, Lagosz M, Gorecka D, Zielinski J. The adequacy of oxygenation in COPD patients undergoing long-term oxygen therapy assessed by pulse oximetry at home. *Eur Respir J* 1994;7:274–278.
4. Steiger JH. Tests for comparing elements of a correlation matrix. *Psychol Bull* 1980;87:245–251.
5. Decker MJ, Arnold JL, Haney D, Masny J, Strohl KP. Extended monitoring of oxygen saturation in chronic lung disease. *Chest* 1992;102: 1075–1079.
6. Morrison D, Swarski KM, MacNee W. The adequacy of oxygenation in patients with hypoxic chronic obstructive pulmonary disease treated with long-term domiciliary oxygen. *Respir Med* 1997;91:287–291.
7. Sliwinski P, Lagosz M, Gorecka D, Zielinsky J. The adequacy of oxygenation in COPD patients undergoing long-term oxygen therapy assessed by pulse oximetry at home. *Eur Respir J* 1994;7:274–278.
8. Schenkel NS, Burdet L, Murald B, Fitting JW. Oxygen saturation during daily activities in chronic obstructive pulmonary disease. *Eur Respir J* 1996;9:2584–2589.
9. Pilling J, Cutaia M. Ambulatory oximetry monitoring in patients with severe COPD. *Chest* 1999;116:314–321.
10. Leggett RJE, Flenley DC. Portable oxygen and exercise tolerance in patients with chronic obstructive pulmonary disease (COPD) and asthma. *Am Rev Respir Dis* 1987;136:225–244.
11. Woodcock AA, Gross ER, Geddes DM. 1981. Oxygen relieves breathlessness in "pink puffers". *Lancet* 1981;i:907–909.
12. Bradley BL, Garner AE, Billiu D, Mestas JM, Forman J. Oxygen assisted exercise in chronic obstructive lung disease: the effect on exercise capacity and arterial blood gas tensions. *Am Rev Respir Dis* 1978; 118:239–243.
13. McDonald CF, Blyth CM, Lazarus MD, Marschner I, Barter CE. Exertional oxygen of limited benefit in patients with chronic obstructive pulmonary disease and mild hypoxemia. *Am J Respir Crit Care Med* 1995;152:1616–1619.