showed significant survival benefit with continuous O_2 therapy (Table 3), reflecting the reduced overall mortality associated with this treatment. Generally patients with hypoventilation and relatively poor pulmonary function—high arterial P_{CO_2}, low pH, low nocturnal oxygen saturation, low FVC, and high FRC—showed increased survival with continuous O_2 therapy. The same was true of patients with more severe brain impairment of neuropsychological testing and of patients who demonstrated high levels of mood disturbance. These results could be synthesized to reach the conclusion that the effect of continuous O_2 therapy was most striking in the sickest patients. On the other hand, it was patients with the least disturbed pulmonary hemodynamics—relatively low mean pulmonary artery pressure and pulmonary vascular resistance—and relatively well preserved exercise capacity who showed benefit from continuous O_2 therapy. Thus the composite patient showing the most benefit from continuous O_2 therapy would have relatively severe derangements of life quality and brain and lung function but relatively mild disturbances of pulmonary hemodynamics and exercise capacity.

Although there was overlap between subgroups showing benefit from continuous O_2 therapy, this overlap was never total. For example, of the 95 patients with baseline pH under 7.40, 24 also had arterial P_{CO_2} less than 43 mm Hg, and of the 107 patients with baseline pH over 7.40, 35 had arterial P_{CO_2} greater than 43 mm Hg.

Most of the differences in mortality noted in Table 3 that we have cited as significant were significant at the 5% level. It might be argued that these differences are not impressive considering that we made many statistical comparisons and that some therefore might attain these levels of significance in the absence of a difference between nocturnal O_2 and continuous O_2 therapy groups. We do not believe that this explains the results shown. Subgroups with high arterial P_{CO_2}, low pH, and more serious mood disturbance showed differences in mortality that were an order of magnitude more significant than those likely to be achieved by chance alone. Groups of independent variables, such as those concerning hypoventilation and lung function, showed concordant differences in mortality that would have been unlikely had they been due to chance. Finally, too many of the variables shown in Table 3 showed $P < 0.05$ to be due to chance; the items shown were selected from analysis of the characteristics shown in Table 2, and probabilities of less than 5% occurred in many more than 5% of the subgroups tested.

The reason for the decreased mortality associated with continuous O_2 therapy is unclear. Of the numerous physiological and psychological variables measured during the study, only two showed a significant treatment-related change with time. Hematocrit value decreased in patients on continuous O_2 therapy but not in those on nocturnal O_2 therapy. Although this result is in accord with the results of animal studies (23), the decline in hematocrit values in the continuous O_2 therapy group was small, averaging 9.2% at 18 months, and assigning any clinical significance to a change of this magnitude is difficult. Overall mortality (Table 3) was very similar in patients with high and low hematocrit values at baseline; having a low hematocrit value at baseline was not associated with increased survival. Further, though continuous O_2 therapy lowered hematocrit values, it appeared to decrease mortality in patients who entered the study with low hematocrit values (Table 3). It appears therefore that although continuous O_2 therapy decreased hematocrit values and increased survival, there is no evidence that these results are related to one another.

Pulmonary vascular resistance also showed a differential effect of treatment, which is also consistent with animal studies showing that intermittent normoxia does not reverse anatomical evidence of hypoxia-induced pulmonary hypertension whereas continuous normoxia does (23). The treatment-related change in pulmonary vascular resistance was more substantial than the hematocrit change, and the 11% decline in resistance seen in the continuous O_2 therapy group may have been partially responsible for its longevity. This is not supported by examining mortality data in relation to pulmonary vascular resistance (Table 3). Although patients who entered the study with high pulmonary vascular resistances had relatively high overall mortality, patients with a low baseline pulmonary vascular resistance showed a mortality benefit from continuous O_2 therapy, whereas those with high resistance did not. The effect of change in pulmonary vascular resistance on mortality also suggested that changes in resistance were not the cause of the lower mortality in patients on continuous O_2 therapy. The median change of pulmonary vascular resistance for 101 patients was a decrease of 20 dyne/s · cm^5 at 6 months. Of patients with a greater decrease 14 subsequently died, nine in the nocturnal O_2 therapy group and five in the continuous O_2 therapy group. Of patients who demonstrated a smaller decrease in pulmonary vascular resistance, nine subsequently died, all from the nocturnal O_2 therapy group. Thus, when both groups were combined, patients with large decreases in pulmonary vascular resistance tended to have a greater mortality than patients with small decreases. Further, it appeared that continuous O_2 therapy had more striking beneficial effect in the patients with small decreases of pulmonary vascular resistance. These data strongly suggest that although continuous O_2 therapy reduced both mortality and pulmonary vascular resistance, the two phenomena were not related.

The present study may be compared with others in which the effects of oxygen therapy have been examined through testing of patients before and after some months of treatment (2-6, 9, 10). Qualitatively, our results are similar. When nocturnal O_2 and continuous O_2 therapy groups were combined, oxygen therapy apparently resulted in a fall in hematocrit value and pulmonary vascular resistance and improvements in neuropsychologic function and the patients' perceptions of their quality of life. However, changes were not large, averaging about 10% in all instances, and whether even these changes were in fact due to oxygen is uncertain. It is entirely possible that these improvements, especially those of quality of life, were due not to oxygen but to the more intensive medical