to die during their sleep at all. Their study was a long-term follow-up study of mortality in treated and untreated sleep apnea patients. They found that there was excess mortality in the group that was untreated if they had a lot of apneas and were less than 50 years of age. The studies complement each other and do not necessarily contradict one another.

The second comment by Kryger et al that deserves response is the implication that we believe that sleep apnea patients should always die during sleep. I believe that this is an exaggeration of our contention, but it is reasonable to think that they would die during their sleep at a rate higher than a control population and we did not find that. Thus, this was a surprising finding but that does not make it incorrect, invalid or not worthy of report.

Thirdly, Kryger et al imply that we said that patients with the sleep apnea syndrome should not be treated. I cannot find anywhere in our paper or our editorial where we mentioned whether patients should be treated or not. It is clear that the decision as to whether to treat the patient with sleep apnea syndrome depends upon more than the expectation of excess mortality. Symptoms such as sleepiness, headache, hypertension, etc., are the usual indication for therapy. Kryger et al have read something into our manuscripts that we never said. We agree that symptomatic patients with the sleep apnea syndrome and an apnea index exceeding 20 should be treated. In fact, all of the patients in the study by He et al were referred to a sleep laboratory because of a syndrome. The syndrome implied symptoms, and these symptoms should be treated. Whether completely asymptomatic, heavy, snoring men should be treated just because the apnea index exceeds 20 is another matter entirely. We are not sure that the indication for treating people based upon a number of apneas alone is correct in 1989.

A Jay Block, M.D., F.C.C.P., and R.J. Gonzalez-Rothi, M.D., F.C.C.P., VA Medical Center, Gainesville, FL

To the Editor:

I read with great interest the two recent articles and related editorial on sleep apnea and mortality.1,4 The increasing healthcare expenditure on diagnosis and treatment of sleep apnea, the morbidity and even mortality associated with treatment, necessitate careful study of the natural history of this disorder. The two reported studies on the mortality of sleep apnea, from Detroit1 and Gainesville,4 produced conflicting results; however, neither study does justice to the topic under investigation. Methodologies and conclusions demand further explanation.

A critical methodologic requirement for any survival study is that the population under investigation be clearly defined, and that a consecutively-seen group of patients be followed for an appropriate period of time, which most commonly is accepted to be five or ten years. Both of these requirements appear to have been poorly met by each study.

The editorial, written by the authors of the Gainesville study, notes that only 55 percent of eligible patients in the Detroit study were included in the final analysis.1 Although the Gainesville group state: “Complete follow-up was obtained on all patients in this study . . . ”, they report a mean follow-up of 90 percent of all eligible patients due to medical records that were not suitable for review.1 As there were only 13 deaths, if the 14 patients that were not included had all died, the conclusions of the group may well have been very different.

The Detroit group did not explain why there were only 22 deaths out of 385 patients of mean age 51 years, who were reportedly followed for up to eight years. Unfortunately, the mean or median follow-up time was not reported by the authors, but it is most likely that the median follow-up time was less than five years, a much shorter time than we are led to believe from the data as presented. The relatively short follow-up time might, in part, explain the relatively small number of deaths reported.

Similarly, the mention of five and eight years of follow-up by the Gainesville group is misleading. They stated: “Kaplan-Meier distributions of all patients over the eight-year study period . . . ”, and repeatedly emphasized the five year nature of their study, both in the original article and editorial, but they also do not give the mean or median follow-up time of their patients. Their data suggest that the median follow-up time is likely to have been less than 2.5 years.

The Gainesville group state in their abstract: “There were no statistically significant differences in mortality between the two groups.” This statement is also misleading, as it implies that similar groups were being compared, whereas the mean age at death of the controls was 66 years, compared with the mean age at death of 50 years for sleep apnea syndrome patients. In addition, the control group (according to the authors) had significantly more life-threatening disease. Perhaps a more meaningful statement by the authors might have been “There were no statistically significant differences in mortality between a younger, healthier group of sleep apnea patients compared with an older, less healthy control group.” The median age at death for the general population in 1984 was 78.2 years; much higher than the mean age at death of 50 years for the sleep apnea patients. The mean or median age at death of the Detroit group’s sleep apnea patients was also not reported but would be of interest.

One interesting point that was not discussed by either group was the fact that the treated sleep apnea patients had a higher death rate than the untreated group in both studies. This could reflect either ineffective treatment or, more likely, might reflect the greater severity of disease. The Detroit group indicated that the high mortality seen in their patients with UPP may be due to a loss to follow-up. Yet the Detroit group specify that 78 of their 96 UPP patients had subsequent follow-up polysomnography, and follow-up of this group of patients has previously been reported.2 A more likely explanation why there were so many deaths in the UPP group would be that this group was followed more closely and, therefore, more deaths were reported. Patients treated by other means were more likely to have been lost to follow-up; therefore, their deaths go unreported. In view of their large group of essentially “untreated” patients who had a lower mortality, it is also hard to accept the explanation that the ineffective treatment of the UPP patients was responsible for the high mortality quoted.3

It is clear that there are many methodologic and reporting errors in both these papers. The Gainesville group stressed the importance of “multicenter cooperative prospective longitudinal studies”. However, because of the morbidity associated with this disease, it is unlikely that such studies will be able to be performed in untreated patients; therefore, we will continue to be dependent upon retrospective studies in obtaining data on such patients. These two papers illustrate the need for careful collection and analysis of data, and one would hope that the “waters will not be muddied” by poorly performed mortality studies. Both of the reported mortality studies are more similar in their findings than the conclusions of the authors would suggest. As both studies indicate, patients with sleep apnea are liable to early death, whether or not it occurs during sleep. The clinician must not be discouraged from “aggressive therapeutic intervention”, as the Gainesville group implied. Additional information is needed to more clearly demonstrate the exact mortality associated with this disease. Despite the deficiencies of these studies, they are both to be commended for raising awareness of the issues regarding the mortality of sleep apnea.

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REFERENCES

2. Gonzales-Rothi RJ, Foresman GE, Block AJ. Do patients with sleep apnea die in their sleep? Chest 1988; 94:531-38

To the Editor:

We very much appreciate Dr. Thorpy's comments on the article and editorial which were recently published in Chest on mortality and sleep apnea. Some of his concerns regarding potential shortcomings in each of the studies are well taken, but we feel that some issues and criticisms raised by the letter deserve clarification and response.

First of all we agree—as he stated—that a critical methodologic requirement for any survival study is that the population under investigation be clearly defined, which we extensively did in our paper under the subheadings "Type of Study, Patient Population, Patient Categories" in the Materials and Methods section and later under "Vital Statistics" in the Results section.

We also wholeheartedly agree that for a population study to be methodologically appropriate, patients should be seen consecutively. The patients in our study were all seen consecutively. While we would also agree that it is generally desirable to follow a group of patients in any population study for as long as possible, we obviously could not "choose" how long our patients were followed; this was, afterall, a retrospective study. It should be noted that the follow-up time of five to ten years that you suggest as "appropriate" is perhaps somewhat arbitrary. As you know, the "appropriate" length of follow-up of mortality from any potentially lethal condition can be based on a "cause-effect" hypothesis of what is likely to cause death from that condition. There are several well done population studies, for instance, that look at one year mortality from sudden death after myocardial infarction. Is one to say that a one year follow-up is not "appropriate" for such population studies? For that matter, does anyone know how long it takes to die from sleep apnea syndrome once it is diagnosed? If one hypothesizes that apnea patients might die in their sleep as a result of hypoxemia, arrhythmias, and episodic pulmonary hypertension (as has been implied by many authors on this subject), it is not altogether outlandish to suspect that increased mortality might be seen with shorter durations of follow-up.

Dr. Thorpy's statement that we do not provide mean follow-up time for the patients in our paper is unwarranted. We refer to Table 1 on page 533, where mean and range of follow-up for each group of patients are quite clearly stated. This information is also included verbatim in the body of the text in the Results section. Along the same lines, he also comments that "the mention of five and eight years of follow-up by the Gainesville group is misleading." We could not recall having ever made such a statement, and even after thoroughly re-reading our paper, we frankly could not find specific mention of "five or eight years of follow-up" anywhere. We did quite outrightly state (both in the abstract and in the first sentence of the Methods section) that our study spanned an eight year period between July 1978 and June 1986, and it is possible that these statements could have been either misread or, alternatively, misinterpreted.

Dr. Thorpy expressed concern that by having excluded 14 patients from our study because their records were unsuitable, we might have biased the findings in our study. We did not include the records of those patients in our study for various reasons: 1) many did not meet criteria of symptoms clinically suspect of sleep apnea; 2) in some patients a sleep study had been insisted upon by the patient or by other physicians (not necessarily from our group) to evaluate abnormal breathing "spells" or undue sleepiness in patients which turned out not to have sleep apnea (i.e., narcolepsy, seizures, pseudo-seizures, "choking spells", Cheyne-Stokes respirations, mental retardation, etc); 3) some were pediatric patients; and 4) some were coded by ICDMA9 diagnoses under "Pickwickian syndrome" but never had confirmatory sleep studies. For these reasons we felt justified in not including these records as suitable for review for our study.

We feel confident that in our study we found no statistically significant differences in mortality between the group of apnea patients and control subjects. The mean ages of the two groups to begin with were not statistically different, and in this sense it could be said that the two groups being compared were similar. The fact that the mean age of patients who subsequently died from each respective group might have differed should not be taken to mean that the original groups being compared were therefore dissimilar, or that the comparisons were therefore invalid or misleading. Predictably, in observational population studies, death is a variable beyond the control of the investigator, as is the age of dying. The differences in age of dying between control subjects and apnea patients is an interesting point that Dr. Thorpy raises and one which merits pursuit in future studies with larger numbers of patients.

Dr. Thorpy also commented that we failed to discuss "the interesting fact" that the "treated" apnea patients had a higher mortality than the untreated group of apnea patients in our study. We did not feel this point merited discussion as a 10 percent ("treated") apnea vs 9 percent (untreated) mortality could hardly be interpreted as a significant difference in death rate between two groups.

Dr. Thorpy also stated that "the clinician must not be discouraged from aggressive therapeutic intervention" as the Gainesville group implied." We quote directly from the conclusion in our article: "Whereas patients with sleep apnea syndrome may exhibit disturbingly severe arterial desaturation and associated dysrhythmias, the clinical impression extracted from this series would suggest that nocturnal sudden death is not as imminent in these patients as our clinical intuition might have previously led us to believe. Therefore, the urgency, timing, and indications for aggressive therapeutic interventions in sleep apnea syndrome, particularly those calling for surgically emergent approaches need to be revisited." We would submit that this statement is clear, that it is well-supported by our data, and that when not taken either out of context or misinterpreted is not likely to be either misleading or discouraging to the treating clinician.

In conclusion, we should perhaps make clear that our personal clinical intuition and bias has always been that patients with sleep apnea syndrome are at increased risk for dying. The intent of our study, however, was to begin to probe that hypothesis with facts and not with suppositions or self-fulfilling prophecies. Our study has shortcomings which we readily acknowledged in both the article and in our subsequent editorial published in Chest. We make no apologies for our findings or conclusions. We contend that both our study and the study by He and co-workers are valid in that they have raised important questions which merit further definition. That these studies are not without shortcomings should neither invalidate them nor open them to undeserved criticisms. In fact, at the risk of "muddying the waters", we are encouraged by the