Women and Chronic Obstructive Pulmonary Disease: Does Sex Influence Survival?

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for sleep medicine research. These regional comprehensive sleep centers will be involved in: research training for both basic and clinical research; providing cores for basic, translational, and clinical research; being the anchors for multicenter clinical research, such as clinical trials and genetics; and creating a data coordinating center. The sleep medicine field has not yet benefited from support for clinical research networks similar to those that have stimulated asthma, chronic obstructive pulmonary disease, and acute lung injury research. Thus, the proposed network will accelerate progress in sleep research where there is a dire need for the rigorous clinical trials and genetic epidemiologic research that have effectively advanced other areas in pulmonary medicine.

The IOM recommendations represent a major opportunity for pulmonary medicine and other disciplines which have a stake in this emerging, exciting interdisciplinary field. As interdisciplinary centers evolve in our academic centers, there will be a need to create career paths for individuals trained in sleep medicine, some of whom will also be pulmonologists. The research opportunities in this area are major. The growing recognition of the importance of sleep disorders outlined in the IOM Report will spur additional clinical activity. The vision laid out can, however, only be accomplished if existing models, whereby sleep medicine is simply a “cash cow” to support other areas in pulmonary medicine or other disciplines who have taken control of the sleep center, becomes a thing of the past. There is a larger, bolder, less parochial vision laid out in this report that leads to addressing the unmet public health need of undiagnosed, unrecognized sleep disorders and sleep deprivation.

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References

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In recent years, chronic obstructive pulmonary disease (COPD) has become an increasing problem among women. In the United States, the absolute numbers of COPD cases, hospitalizations, and deaths among women have exceeded those among men (1). Similar trends have been observed in Canada (2), the United Kingdom (3), Finland (4), and other countries. This has occurred

| TABLE 1. ATTRIBUTES OF INTERDISCIPLINARY TYPE I, II, AND III ACADEMIC SLEEP PROGRAMS |
|---------------------------------------------|---------------------------------|
| Interdisciplinary Sleep Programs            | Focus                            |
| Type I                                      | Clinical core specialties         |
|                                             | Increases awareness of sleep medicine among health care professions. Requires educational programs for medical students and residents in primary care. Includes representation from internal medicine, neurology, psychiatry, otolaryngology, pediatrics, and nursing. |
| Type II                                     | Clinical, training, research      |
|                                             | Provides optimal education, training, and research in Somnology and Sleep Medicine. Accredited fellowship program in Sleep Medicine. Basic or clinical research program. |
| Type III                                    | Regional comprehensive centers   |
|                                             | Serves as a center for public health education, training for clinical care and research, basic research, patient-oriented research, translational research, and clinical care. Regional coordinator for the proposed National Somnology and Sleep Medicine Research and Clinical Network for education, training, mentoring, clinical care, research, clinical research studies, and large-scale population genetics studies. |

a methodologic mentor in the home institution of the trainee with a sleep mentor in another institution. There is clearly a need to improve the pipeline, particularly of physician-scientists, and creative strategies need to be implemented and encouraged by the pulmonary community.

The Report identified sleep research as a prototypical interdisciplinary endeavor with the strong potential to be included in NIH Roadmap initiatives that highlight translational and transdisciplinary medicine. The science of sleep medicine, or “somnology,” requires involvement of individuals from many different backgrounds. As with any interdisciplinary program, departmental or divisional “silos” represent barriers to progress (4). The Report calls for interdisciplinary sleep centers to be established in all of the nation’s 125 academic centers. It proposes that three types of centers to meet the varying goals of different institutions (Table 1). The proposed regional comprehensive centers (type 3) are based on the Cancer Center model, and it is envisaged that they will form the basis for a national network
Despite evidence that physicians have historically been less likely to diagnose COPD in women compared with men (5), an important question is whether sex differences exist in the development, progression, and outcomes of COPD (6). These differences, if present, may provide valuable information on risk factors, treatment, and prognosis of COPD.

The increasing prevalence of COPD among women in the developed world is thought to be related to the historic increase in smoking among women in these populations. The question remains, however, whether women are intrinsically more likely to develop COPD than men, with some evidence suggesting that they are, but other evidence indicating that they are not (7, 8).

A separate question is whether the prognosis of COPD varies between men and women. In population-based samples, women live longer than men (9). Whether this is true among people with COPD is not completely clear. In a recent review of the topic, Chapman concluded, “There are documented differences in health care use between men and women who have COPD, but too few studies have been done to allow conclusions to be drawn about the impact of sex and gender on the prognosis of the disease” (10).

The article by Machado and colleagues in this issue of the Journal (pp. 524–529) (11) found that women with COPD who were oxygen-dependent died more quickly than men. After adjusting for covariates, the risk of death among women increased. The initial question one must ask in evaluating a study is whether the findings are real and if they make sense. In this case, there were several inclusion and exclusion criteria for the study. The inclusion criteria were an FEV1/FVC less than 0.70 and treatment with long-term oxygen therapy. Patients who met these criteria but who died within 6 months of starting oxygen were excluded. Current smokers (either by self-report or physician judgment) were not included because they were not eligible for long-term oxygen therapy. We don’t know whether the decision-making processes to place patients on oxygen were similar between men and women. We also do not know whether a similar proportion of men and women dropped out or died within 6 months, thus not qualifying for the study. If the population excluded by these criteria was similar for men and women then it is of interest that the women in the study were significantly younger than the men, suggesting that women treated for COPD in this hospital had developed COPD at an earlier age than men.

A second potential bias in the study is that adherence to treatment may have been different between men and women. The observed survival difference could be seen if women were less likely to use their oxygen as prescribed than men. A recent review of 164 studies of adherence to medical therapy did not detect a sex difference (12), making this explanation less likely, although still possible.

If the findings of this study are real and represent a true difference in COPD outcomes between men and women, then it is important to understand why these differences are occurring and whether they might be amenable to an intervention. One explanation for worse survival among women might be that some of the systemic complications of COPD, such as the muscle dysfunction or depression, are more common in women and that these lead to worse outcomes. In two recently published studies of patients with COPD, women had almost three times the prevalence of depression as men (38 vs. 13%) (13) and twice the prevalence of fat-free body mass depletion (40 vs. 20%) (14). While we do not know whether these complications were increased in the Machado and colleagues’ study, it is plausible that the observed differences may have been related to these or other COPD-related complications that differ between sexes.

Does sex influence survival in COPD? This is still an open question. The study published in this issue of the Journal suggests that women with COPD who are on oxygen may die more quickly than men (11). Whether this observation holds true in other cohorts with differing severity of COPD is yet to be determined. Careful analysis from both clinical data and observational trials will shed more light on this important question and, it is hoped, provide guidance for how to better intervene in the care of our patients with COPD.

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