



educational grants and travel assistance from various pharmaceutical companies producing drugs for the treatment of psychiatric illness, but not in direct relation to this article.

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# Sex or body size? Selection of dialysis type revisited

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In their Research Letter appearing on page 818, Christine Florakas and colleagues<sup>1</sup> describe a reconsideration of conclusions drawn in a previous study, which had suggested a gender bias in the selection of type of dialysis in Canada. In their earlier study,<sup>2</sup> published in *CMAJ* in 1994, these authors found that, for the period 1981 to 1991, women were more likely than men to undergo peritoneal dialysis. That study was based on data from the Canadian Organ Replacement Registry (CORR), for variables available at that time.

For the new analysis, the authors used data for 4467 patients who began therapy in 1993 and 1994, including variables (specifically weight, height and body surface area) that were not included in the CORR data collection before 1993. Using logistic regression analysis, they show that selection of type of dialysis in 1993 and 1994 was most likely determined by patient weight, not sex. The nephrology literature from 1993 and 1994 suggested that lower body weight was associated with better success of peritoneal dialysis.<sup>3</sup> Thus, given the educational material and prevailing practices at the time, it would appear that the patients who, under the guidance of their physicians, selected peritoneal dialysis did so appropriately, as they were of lower weight than those who chose hemodialysis. Interestingly, there was no association with body surface area, which is also derived from weight and height measurements. The logistic regression analysis thus isolated the independent effect of weight on type of dialysis when body surface area, sex and other variables were entered into the model.

This new analysis highlights the importance of includ-

ing in such studies all of the variables that might have an impact on the outcome of interest. It also heightens our awareness that sex is often a marker for other variables (e.g., weight, height, body surface area, muscle mass and socioeconomic status). When designing statistical models, researchers must define, *before* the analysis, all of the variables that might affect the outcome of interest, so that confounding can be minimized.

The possibility of gender bias continues to be raised in the context of treatment for many diseases, so it behoves both researchers and clinicians to continually review both study results and treatment practices with respect to this determinant. For example, an analysis of data from the BC Cardiac Registry showed that women had a much higher risk of illness and death during cardiovascular surgery than men,<sup>4</sup> and there is substantial evidence for this type of bias with respect to outcomes of cardiovascular disease.<sup>5-7</sup> However, further analysis — in particular, a review of other confounders — has raised a number of issues and insights. Women are often referred later than men for invasive procedures; they often present with atypical chest discomfort, which leads to a delay in diagnosis and treatment; the instruments for angioplasty and surgical procedures are usually designed for and tested on men; and differences in vascular anatomy (e.g., vessel calibre) have been demonstrated.<sup>6,7</sup> Any or all of these factors might account for differences in outcome between men and women. Thus, while sex may be a marker for poorer outcomes for cardiovascular disease and related surgery, it is confounded by potentially modifiable variables (e.g.,



time of diagnosis and changes in technology or tools). Review of issues such as these suggests the potential utility of a randomized controlled trial to compare outcomes for men and women referred for surgery or other treatment according to the same criteria and treated with appropriately designed instruments, according to a set protocol. Registry data often suggest areas for further investigation and raise questions about current practices and attitudes, but they should not be the basis of definitive conclusions, especially in situations of potential gender bias.

There is at present an imbalance between men and women in the population of patients with end-stage renal disease in Canada: the current ratio of men to women is 60:40.<sup>8</sup> In contrast, US dialysis registry data indicate that men and women are more equally represented in that country.<sup>9</sup> One potential explanation is that in Canada there is a gender bias in acceptance to treatment programs, but other explanations are possible. Given that indicators of renal function, such as creatinine level, are related to muscle mass and that the threshold creatinine level for referral from a general practitioner to an internist or nephrologist is around 350–500  $\mu\text{mol/L}$ ,<sup>10</sup> it is possible that many women are dying from complications due to renal failure without their need for dialysis being recognized. A creatinine level of 500  $\mu\text{mol/L}$  in a 50-year-old woman weighing about 62 kg would reflect creatinine clearance of approximately 6 mL/min, a level at which dialysis should be initiated. At lower levels of renal function, fatal dysrhythmias, volume overload and heart failure may occur. Thus, the difference in the proportions of men and women receiving dialysis therapy in Canada may reflect gender bias not in acceptance to treatment programs, but rather in referral patterns before treatment.

In summary, analyses of data for multiple variables from large population databases are susceptible to confounding. The modelling techniques for such analyses need to be clarified, and investigators should clearly identify, before the analysis, all of the variables that might affect the outcome of interest. If all of these variables are not available for analysis, then any conclusions must be considered in the context of the missing information. The issue of gender bias in medical practice continues to be discussed, and we as researchers and clinicians need to delineate those variables that confound sex in regard to therapy or diagnostic testing to clarify if changes in outcome could be brought about by changes in attitudes or by changes in techniques affected by other variables for which sex is only a marker.

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