Response to the letter to the editor for “Obstructive Sleep Apnea and Risk of COVID-19 Infection, Hospitalization and Respiratory Failure”

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Dear Editor,

We thank Dr. De Kruif and colleagues for their interest in our recent brief report about the risks of COVID-19 related to obstructive sleep apnea (OSA) [1]. They raise important insights related to the limitations inherent in analyzing large administrative data sets, several of which we had highlighted in our discussion. We appreciate the opportunity to clarify points raised by their letter and provide further comments about the reliability of these data in evaluating for a relationship between OSA and COVID-19 risks.

The most important concept in interpreting retrospectively analyzed administrative data is to recognize the distinction between evaluating point prevalence and relative risk. Not all individuals in this cohort have undergone a systematic assessment protocol for OSA, so the prevalence of OSA in this cohort is clearly less than its actual prevalence. It is well known that OSA is severely under-recognized and undertreated throughout the world with actual prevalence rates much greater than community diagnosis rates [2]. The objective of our study, however, was not to ascertain the absolute prevalence of OSA or COVID-19 in our region, but to examine the relationship between them. As the authors note, we pointed to published data showing that OSA coding in administrative data is highly

specific to true diagnosis, not that it is highly sensitive. Because our analysis was based on odds ratios, as long as the approach to identifying OSA in a population is reasonably consistent and there is a low rate of false-positive diagnoses coded, odds ratios calculated for subgroups will be reasonably reliable even when the odds for each subgroup may be under- or overestimated. This principle is one of several reasons that risk estimates from large observational datasets often accurately match those from large randomized studies and, in the case of epidemiologic questions, may be more accurate [3, 4].

The registry indeed contained the full system cohort of over 5 million records, whereas specific diagnoses of interest in our study (COVID-19, OSA, diabetes, hypertension, body mass index, hospitalization, and respiratory failure) were included based exclusively on codes entered between the study inclusion dates. This restriction was used to limit the effect of temporal trends in the sensitivity and specificity of administrative coding and to ensure that diagnoses were contemporaneous. Because the statistics of interest to address the study objectives are ratios and not absolute rates, the use of date limits supports good accuracy. With respect to the analysis of covariates and the multivariate models, age was dichotomized at 50 because that was the approximate median age. As shown in the Table, we adjusted the models for hospitalization and respiratory failure for diabetes, hypertension, and BMI to address the possibility of a confounding pattern in which the effects of those factors on COVID-19 outcomes could be mediated through OSA. The fact that all the individuals in these models were recently hospitalized in one of our system hospitals allowed these variables to be consistently ascertained and recorded (e.g., height and weight measurement for accurate, contemporaneous BMI measurement). We did not construct a multivariable model of COVID-19 infection risk because accurate, contemporaneous measurement of those variables was not similarly available. We selected these covariates for the adjusted models because they are the variables that have shown the clearest, independent risk effect on COVID-19 outcomes in other large population studies

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[5]. There are likely to be numerous other important factors influencing COVID-19 outcomes. Like many of the analyses published early in the pandemic, we characterize our brief report as a first step in exploring a complex phenomenon and look forward to seeing it refined by further work.

The fundamental and important finding in the data we reported was neither the extreme precision of our reported point estimate for OSA prevalence nor that we have excluded the possibility of any residual confounding, but instead that these data offer compelling evidence that individuals with OSA are at much greater risk for clinical COVID-19 infection and that after adjustment for the other major morbidity risk factors, they experience worse outcomes. We agree with Dr. De Kruif and colleagues that these results evoke a sense of alarm and believe they justify recommending that individuals with OSA scrupulously adhere to recommendations from public health authorities to minimize their risk of infection.

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