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BRIEF REPORT

Understanding the Relationship Between Antiviral Prescription Data and COVID-19 Incidence in New York City: A Retrospective Cohort Study

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The coronavirus disease 2019 (COVID-19) pandemic has caused more than 675 million confirmed cases and nearly 7 million deaths worldwide [1]. While testing for COVID-19 was initially centered in health care facilities, with required reporting to health departments, it is increasingly being performed in the home with rapid antigen testing [2]. Most at-home tests are self-interpreted and not reported to a provider or health department, which could lead to delayed reporting or underreporting of cases [3]. As such, there is a strong possibility that reported cases may become a less reliable indicator of transmission over time.

Keywords. antivirals; COVID-19; modeling; public health.

In December 2021, nirmatrelvir/ritonavir and molnupiravir received Emergency Use Authorization by the US Food and Drug Administration for the treatment of coronavirus disease 2019 (COVID-19) in high-risk patients [4]. In New York City (NYC), these therapeutics were immediately made available at no cost to eligible residents via pharmacy pickup or free home delivery, allowing for ease of access to antivirals compared with other jurisdictions, where access may have been more limited [5]. We studied the extent to which antiviral prescription trends, identified through a system of centralizing requesting, are indicators, possibly leading indicators, of case trends in the setting of decreased case reporting [6].

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METHODS

Confirmed and probable COVID-19 cases are reported to the NYC Department of Health and Mental Hygiene (DOHMH). At the time of this work, all pharmacies participating in the federal COVID-19 therapeutics program were required to report daily utilization data, which were tabulated and tracked through the Tiberius platform. Data were available from December 29, 2021, to December 31, 2022. We analyzed citywide weekly case counts for all patients 18 years and older from March 1, 2022, to December 31, 2022, a time frame during which antiviral supply consistently exceeded demand. Analysis was performed using R Statistical Software (version 4.2.1) and the R libraries tidyverse, scales, readxl, lubridate, and cowplot [7–13]. Weekly total cases were analyzed to avoid the effect of substantial weekly reporting cycles. Given the absence of periodicity in the data, a linear regression model was performed. Goodness-of-fit plots for the model were analyzed. A receiver operating characteristics (ROC) curve was constructed using the size of the weekly change in prescriptions to predict the direction of that week's case count.

RESULTS

During the study period, 279 815 COVID-19 antiviral prescriptions were filled for patients aged 18 and above. Of these, 17.5% were filled through the NYC DOHMH partner pharmacy, and 82.5% through nonpartner pharmacies. Monthly antiviral prescriptions ranged from 5161 in March 2022 to 45 657 in December 2022. Monthly prescription totals varied from month to month, with no trend noted. A total of 745 669 cases in patients aged 18 and above were reported. Weekly case rates during this period ranged from 40.56 to 346.71 cases per 100 000 residents.

For a given week, the correlation between total cases and total prescriptions was 0.92. Auto- and cross-correlation studies of lagged series showed significant but declining autocorrelations within each type of count and between total cases and prescriptions. The significant correlations occurred for lags of 2 weeks, regardless of whether it was prescriptions or cases that were lagged. No cyclic changes were seen. When the weekly case totals were regressed on the weekly prescription totals, the model had an R^2 of 0.84, implying that ~85% of the variation in case counts may be accounted for by information contained in the prescription count (Figure 1).

We investigated if the direction of weekly changes in prescription totals predicted the direction of changes in case totals. There was a strong concordance, with the direction of weekly changes being concordant in 73% (28/38) of weeks. Considering direction of change in prescriptions as a "diagnostic" test for direction

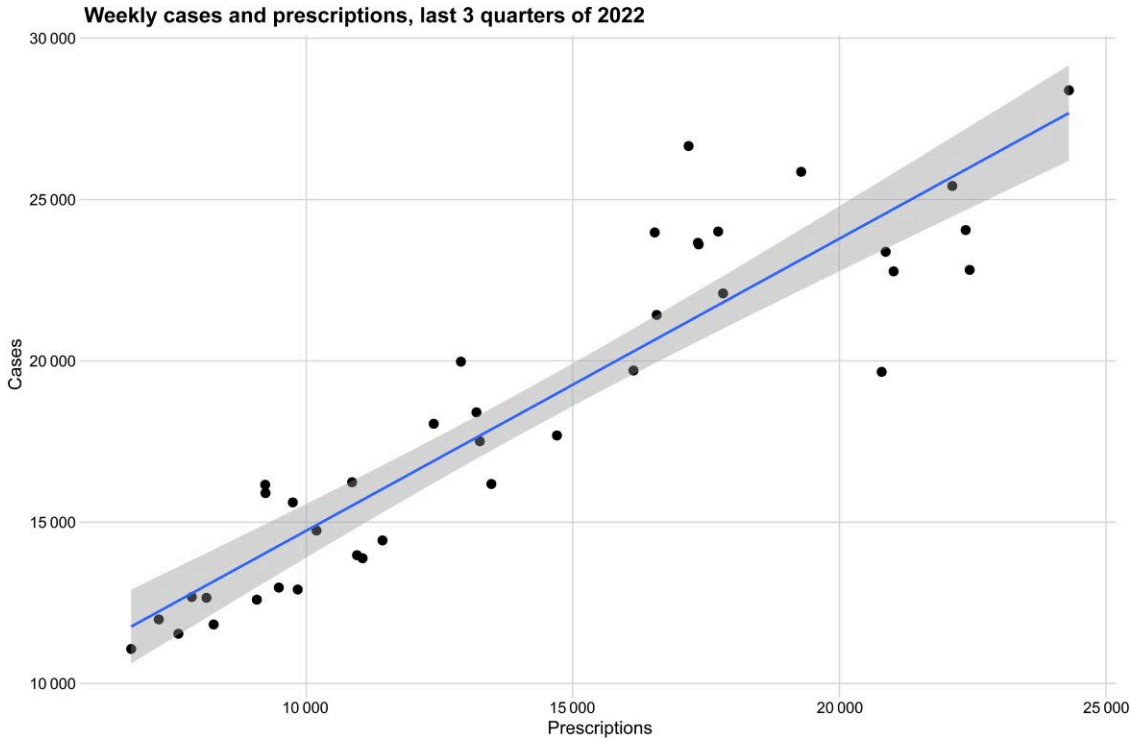

Figure 1. Regression of weekly case numbers on weekly prescriptions. The shaded area is a 95% confidence interval for the line. R^2 for the regression line was 0.84.

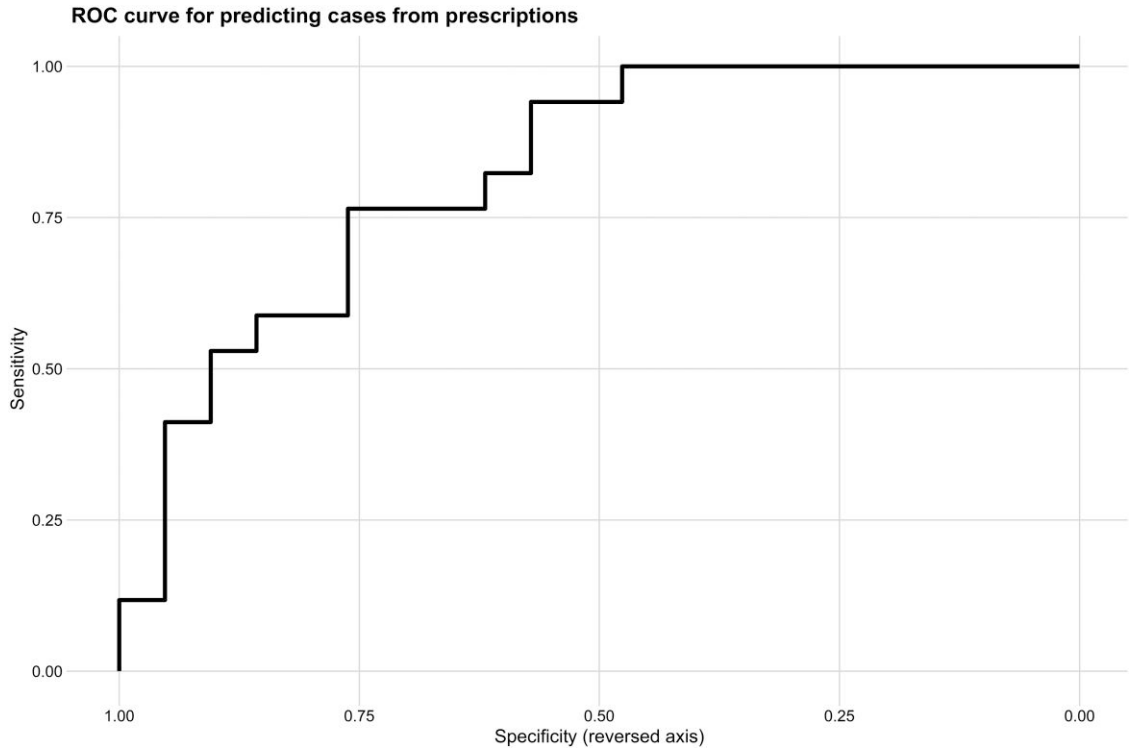

Figure 2. ROC curve for predicting the direction of a change in number of weekly cases from the magnitude of the change in number of weekly prescriptions. The area under the curve is 0.82. Abbreviation: ROC, receiver operating characteristics.

of changes in cases, the sensitivity was 76% (13/17 weeks) and specificity was 62% (13/21). The predictive value of a positive test (ie, increase in prescription count) was also 62% (13/21), and the predictive value of a negative test (ie, decrease in prescription count) was 76% (13/17).

We also investigated if the size of the change in prescription count was predictive of an increase in case counts by constructing an ROC curve (Figure 2). The area below the ROC curve was 82%.

DISCUSSION

In our analysis, we observed a strong correlation between COVID-19 oral antiviral prescription fills and subsequent case counts. This relationship was very strong in relation to case counts within 7 days and remained significant at 14 days. We found that autocorrelation suggested that prescription data were not a leading indicator for future increases in cases and were most strongly associated with the current week's case data. Limitations include the special circumstances of the self-reported pharmacy data collection required during this public health emergency. When medications are dispensed without a timely and complete reporting system, the information gathered will reflect those weaknesses. In addition, prescription counts cannot replace case reporting for collection of all needed public health data. Additionally, the use of antivirals is focused on more high-risk groups and could underestimate case counts in younger or healthier populations. This study also took place in New York City, which could limit generalizability due to variability in therapeutic uptake and access in other jurisdictions. Finally, the limited amount of data, representing only 9 months of weekly totals, did not permit us to do more than describe the behavior of the prescription data. Validation and utility assessment must await additional data collection and may not be possible after transition of COVID-19 antivirals to the commercial market.

As COVID-19 testing moves away from traditional testing locations and into people's homes, new strategies are needed to enhance timely epidemic monitoring. Currently, public health access to pharmacy prescription data is very limited, and avenues for access at this time tend to be circuitous; this leads to delays in obtaining these data, often with significant cost. Currently, the Centers for Disease Control and Prevention has prioritized a Data Modernization Initiative, which will increase lines of communication between public health entities and health care systems. However, this effort does not explicitly call out the important role that complete and timely pharmacy data will have in public health surveillance and forecasting [14, 15]. Our study highlights that rates of oral therapeutic prescribing could represent an early indicator of increasing COVID-19 transmission in a community and highlights the need for expanded public health access to these data. Furthermore, oral antiviral prescriptions may be an indirect marker of higher-risk infections given that oral antivirals are authorized for older individuals and those with comorbid conditions. These findings underscore the importance of improving national integrated health data systems that facilitate access to timely prescription data for public health surveillance and, ultimately, enhanced policy and decision-making.

For the monitoring of trends in prescription dispensing, a system needs the following properties: reporting must be complete or be a representative sample of the full universe of prescriptions; reporting must be at least as timely as reporting of cases; and the impact on prescription demand caused by changes in severity of illness with newer variants of SARS-CoV-2 should be accounted for. Next steps would include validating this model by forecasting future cases and exploring how these data correlate to hospitalization trends given that patients receiving antivirals are at higher risk for severe outcomes. Further research is needed to optimize the addition of prescription data to forecasting models attempting to predict trends in COVID-19 transmission as reported cases become a less reliable indicator.

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Potential conflicts of interest. All authors report no potential conflicts.

Patient consent. This study does not include factors necessitating patient consent.

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