

Tracking Potential COVID-19 Outbreaks With Influenzalike Symptoms Urgent Care Visits

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The 2019–2020 influenza season has had elevated influenza-confirmed hospitalization rates.¹ Simultaneously, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected millions worldwide.² There are open questions about coronavirus disease 2019 (COVID-19) related to its prevalence³ and seasonality.⁴ Many individuals who develop COVID-19 present with influenzalike illness (ILI) symptoms, including fever, cough, or sore throat.⁵ This symptom overlap makes it difficult to differentiate COVID-19 from influenza or other related illnesses without testing, which has limited availability in the United States.⁶ Understanding the degree to which ILI in a community is not due to influenza could help clinicians estimate the risk of COVID-19. The proportion of local current cases of ILI that are influenza-negative could inform clinical care and provide epidemiological insight into the ongoing pandemic.

METHODS

CodoniX is an electronic health record that captures data from ~3000 patients daily from >100 urgent care clinics in 15 states. We evaluated data for patients ≤21 years seen during the months of January, February, and March from 2018 to 2020. We also evaluated COVID-19 data from the same period; however, because there were fewer recorded cases, all ages were used.

We evaluated *International Classification of Diseases, 10th Revision* (ICD-10) codes for discharge diagnoses of fever, cough, sore

throat, influenza, streptococcal pharyngitis, COVID-19, mononucleosis, and respiratory syncytial virus, and we evaluated Logical Observation Identifiers Names and Codes (LOINC) for positive test results. The diagnosis of influenza was based on either a positive test result or the discharge diagnosis. There is no ICD-10 code for ILI, so it was defined as an *ICD-10* diagnosis of fever with cough and/or sore throat without another known cause, such as mononucleosis or respiratory syncytial virus. The distribution of these diagnoses by age range is presented in Supplemental Table 1.

To validate the CodoniX data findings, publicly available ILI, influenza, and COVID-19 data from the Centers for Disease Control and Prevention (CDC) were collected. ILI diagnoses were collected from the CDC's Outpatient Influenzalike Illness Surveillance Network, and CDC COVID-19 data were acquired from the Johns Hopkins University Center for Systems Science and Engineering coronavirus repository. For both of these data sets, all ages were used for analysis. However, influenza data collected from public health laboratories that report as World Health Organization Collaborating Centres and Essential Regulatory Laboratories are stratified by age, so only ages 0 to 4 and 5 to 24 years were used in the analysis.

RESULTS

In both the CodoniX and CDC data, an increase in the ratio of ILI diagnoses to



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Mr Muchmore conceptualized and designed the study, collected data, conducted initial and final analyses, and drafted the initial manuscript; Dr P. Muchmore, Mr Lee, and Dr Alarcón-Riquelme conducted the initial analyses and collected data; Dr A. Muchmore designed the data collection platform and coordinated and supervised data collection; and all authors reviewed and revised the manuscript and approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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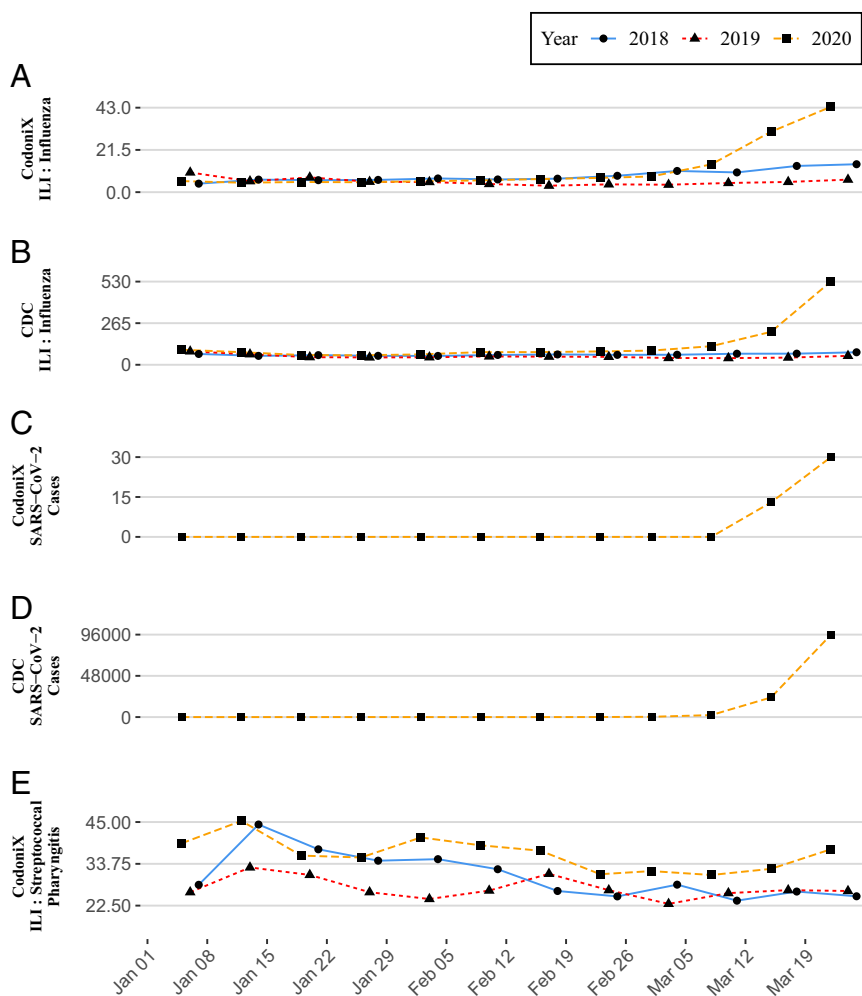


FIGURE 1

Time series of disease ratios along with weekly SARS-CoV-2 positive test results. A, The ratio of weekly CodoniX ILI cases to influenza cases. B, The ratio of weekly CDC ILI cases to CDC influenza-confirmed hospitalizations. C, Weekly CodoniX positive SARS-CoV-2 test results. D, Weekly CDC positive SARS-CoV-2 test results. E, The ratio of weekly CodoniX ILI cases to streptococcal pharyngitis cases.

confirmed influenza cases was observed in late February and early March 2020, which was not evident during the same period in 2018 or 2019. Figures 1 A–D illustrate, for each year, the ILI to influenza ratio and number of COVID-19 cases. Figures 1 A and B suggest an increasing trend in March 2020 that was absent in March of 2018 and 2019, and these temporal patterns match the absolute weekly COVID-19 case incidence seen in both the CodoniX (Fig 1C) and CDC COVID-19 data (Fig 1D). In 2020, the ILI to influenza ratio rose in February, and, with Buishand U test, a change point

during the last week of February ($P = .01$) was indicated. By using an adjusted Mann-Kendall trend test for the same time series, a statistically significant trend ($P < .001$) was indicated (Supplemental Table 2). Figure 1E shows the ratio of ILI cases to streptococcal pharyngitis cases, and Supplemental Fig 2 illustrates a heat map and the clustering of these time series based on a statistical measure of similarity.

DISCUSSION

Our results indicate that, beginning in February 2020, a significant number

of patients receiving ILI diagnoses were infected with a virus other than influenza. This suggests that monitoring the ratio of influenza-negative ILI cases to influenza-positive cases could potentially be used as an early warning system for influenza-negative viral syndromes with features of ILI.

A limitation of our study is that many diseases, including COVID-19, do not always present as ILI. For example, although influenza patients typically present with ILI symptoms, streptococcal pharyngitis patients often do not, so we would not expect the ratio between the two to contain a discernible pattern, which is supported by Fig 1E. However, although describing the clinical presentation of COVID-19 is an ongoing topic of study, recent data indicate it may often present as ILI.⁷ Additionally, although the CDC and CodoniX data exhibit similar patterns, neither constitute a random sample of US residents, and the extent to which they are representative of the entire population is unknown.

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ABBREVIATIONS

CDC: Centers for Disease Control and Prevention
 COVID-19: coronavirus disease 2019
 ICD-10: *International Classification of Diseases, 10th Revision*
 ILI: influenzalike illness
 LOINC: Logical Observation Identifiers Names and Codes
 SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

POTENTIAL CONFLICT OF INTEREST: Dr A. Muchmore is founder and CEO of CodoniX, Inc. Mr Lee is a CodoniX employee. Mr Muchmore and Dr P. Muchmore consult for CodoniX. Drs A. Muchmore and P. Muchmore own stock in CodoniX, Inc.

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